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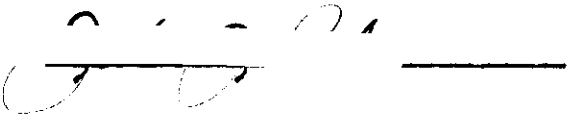

THE FORMATION OF METHYLENE INTERMEDIATES FROM ORGANIC SULFUR COMPOUNDS

A THESIS

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FROM ORGANIC SULFUR COMPOUNDS

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TABLE OF CONTENTS

Page

LIST OF TABLES

LIST OF ILLUSTRATIONS

SUMMARY

The solvolysis of haloforms in basic solution has been shown previously to proceed by a mechanism that includes formation of a methylene intermediate. The mechanism, termed an α-elimination, proceeds as follows:

$$CX_3H + \text{base} \longrightarrow CX_3^-$$

$$CX_3^- \longrightarrow CX_2 + X^-$$

$$CX_2 \longrightarrow \text{products}$$

Chlorodifluoromethane has been found to react with base to yield the difluoromethylene directly, and not to undergo carbanion formation. The reaction of this compound with sodium methoxide in methanol was studied and was believed to give a difluoromethylene intermediate which reacted further to give difluoromethyl methyl ether and methyl orthoformate, and with added sodium thiophenoxide, difluoromethyl phenyl sulfide and a substance believed to be triphenyl orthothioformate but not isolated in a pure form. These products were not formed from a direct S_N2 displacement, as no appreciable reaction took place between the thiophenoxide ion and chlorodifluoromethane unless sodium methoxide was present to bring about the proposed concerted α-elimination.

The mechanism proposed for these reactions is as

follows:

$$CHClF_2 + CH_3O^- \xrightarrow{CH_3OH} CF_2$$

$$CF_2 \xrightarrow{CH_3OH} CH_3OCHF_2 + (CH_3O)_3CH$$

$$C_6H_5S^- + CF_2 \xrightarrow{CH_3OH} C_6H_5SCF_2H + (C_6H_5S)_3CH$$

Since thiophenoxide ion is known to be strongly nucleophilic, it was used in this case to capture the intermediate difluoromethylene, which should be subject to nucleophilic attack. The presence of sodium methoxide caused the thiophenoxide to react as much as 60 times as fast as it would have in the absence of added base. Considering their relative concentrations the thiophenoxide ion was found to be more than 100 times as effective at capturing the methylene as methanol. Difluoromethyl phenyl sulfide was isolated in more than 60 per cent yield in one run in the presence of added sodium methoxide.

The other products of the reaction of sodium methoxide and sodium thiophenoxide with chlorodifluoromethane were high boiling materials that were not characterized definitely, but triphenyl orthothioformate was believed to be present.

To determine the products of the other paths of the reaction sodium thiomethoxide was used, in order to give lower boiling reaction products, which would be easier to separate and characterize. Difluoromethyl methyl sulfide, methyl orthomonothioformate, and methyl orthothioformate

were isolated in 44.2, 6.0, and 28.2 per cent yields respectively based on the methanethiol that reacted. The formation of trimethyl orthothioformate indicates the presence of a sulfur-containing methylene intermediate as in the following sequence of reactions:

$$CHF_2Cl + CH_3O^- \xrightarrow{CH_3OH} CF_2$$

$$CF_2 + CH_3S^- \xrightarrow{CH_3OH} CH_3SCF_2H$$

$$CF_2 + CH_3S^- \xrightarrow{CH_3OH} CH_3S\text{-}C\text{-}F$$

$$CH_3S\text{-}C\text{-}F + CH_3S^- \xrightarrow{CH_3OH} (CH_3S)_3CH$$

Difluoromethyl methyl sulfide was shown to be unreactive under the reaction conditions and therefore incapable of having produced trimethyl orthothioformate. It is unlikely that the thiomethoxide anion would attack any difluorothiomethoxycarbanion that might exist, since the like charges would repel each other. The remaining path is that through a thiomethoxyfluoromethylene. The formation of this methylene would agree with the observed kinetic and synthetic results. In the kinetic study it was necessary to determine the acidity of methanethiol relative to methanol. This was done at varying ionic strengths using the indicator thymol blue. The equilibrium constant was determined for the following equilibrium

$$CH_3SH + CH_3O^- \rightleftharpoons CH_3S^- + CH_3OH$$

The values obtained varied from about 100 to 350 over

the ionic strength range of 0.02 to 0.55. This equilibrium was far enough to the right so that only a few per cent of the methoxide ion existed in runs where methanethiol was in excess. This was sufficient to show the catalytic effect of methoxide ion on the reaction.

The difluoromethyl phenyl sulfide produced in the earlier reactions was a liquid and decomposed unless stored over sodium carbonate. To increase its stability and raise its melting point it was oxidized to the sulfone with hydrogen peroxide in an acetic acid medium. The sulfone obtained melted at 25° and gave a satisfactory elemental analysis and molecular refractivity. The sulfone was studied synthetically to see what products, if any, were produced in the reaction with sodium methoxide and sodium thiophenoxide. In one run benzenesulfinic acid was isolated in over 50 per cent yield, difluoromethyl methyl ether in 39 per cent yield and difluoromethyl phenyl sulfide in over 22 per cent yield based on the reacting sulfone.

A kinetic study showed that sodium methoxide catalyzed the reaction between difluoromethyl phenyl sulfone and thiophenoxide ion. This fact and the products isolated show that the same methylene must be produced here as in the case of chlorodifluoromethane. As the sulfone reacted with methoxide much slower than the haloform (20 times slower at a temperature 15 degrees higher) it was thought that the sulfone might be undergoing a two step α-elimination. To check this the deuterium exchange of the sulfone was studied and

deuteriodifluoromethyl phenyl sulfone was found to exchange deuterium for protium with a rate constant of 9.54×10^{-4} l. mole^{-1} sec.$^{-1}$ at 0° in methanol. This result showed a stepwise α-elimination through a carbanion to be the mechanism of reaction for the sulfone. The deuterium exchange of deuteriodifluoromethyl phenyl sulfone was also studied in water at 0° and the rate constant found was 6.00×10^{-2} l. mole^{-1} sec.$^{-1}$.

These results give a more complete understanding of α-elimination reactions and show in some degree how fluorine substituents on a carbon atom can affect its manner of reaction.

CHAPTER I

INTRODUCTION

In the past few years the research work on the mechanism of solvolysis of haloforms has more conclusively revealed that these compounds react with basic reagents to form methylenes, intermediates different from those generally proposed for organic reactions. The mechanism has been designated as an α-elimination (1). The examples studied have involved the reversible formation of a carbanion followed by loss of halogen to give a dihalomethylene intermediate which can react further to give the observed products. The mechanism is as follows:

$$CX_3H + \text{base} \longrightarrow CX_3^-$$

$$CX_3^- \longrightarrow CX_2 + X^-$$

$$CX_2 \longrightarrow \text{products}$$

The discovery of this mechanism came from the fact that the reaction was much faster than would be expected from the generally accepted S_N2 mechanism (1). As methylene halides are known to react much slower with nucleophilic reagents than do methyl halides, chloroform would be expected

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(1) J. Hine, Journal of The American Chemical Society, 72, 2438 (1950).

to be less reactive toward nucleophilic reagents than is methylene chloride. However, toward the more basic nucleophilic reagents, chloroform was found to be much more reactive (2). While thiophenoxide reacted only slowly with chloroform in the absence of added hydroxide, its reaction rate increased in some cases 1000-fold in the presence of added hydroxide ion (1). These results show that a mechanism other than a direct nucleophilic displacement must be taking place. The second step in the reaction has also been verified by the observation that added halide ions slow the reaction (3). Hine and Dowell found that when sodium fluoride, nitrate and perchlorate were added individually to solutions containing chloroform the basic hydrolysis rates were the same within experimental error for each of these salts. When sodium chloride, bromide and iodide were added individually to the chloroform solutions, the rates of basic hydrolysis were decreased initially. Their explanation was that chloroform was reacting to give a dichloromethylene intermediate which reacted with the added halide ion to form a haloform and thus slow down the disappearance of base. All of these experimental facts support the α-elimination mechanism.

In the haloform series it would be of interest to see

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(2) P. Petrenko-Kritschenko and V. Opotsky, Berichte der deutschen chemischen Gesellschaft, 59B, 2131 (1926).

(3) J. Hine and A. M. Dowell, Jr., Journal of The American Chemical Society, 76, 2688 (1954).

whether any methylene intermediate formed in the α-elimination could be captured and the immediate product of capture isolated directly, as this would give more conclusive evidence for its existence. The products isolated thus far in homogeneous haloform solvolysis reactions are those of further reaction of the dihalomethylene reaction product and in most cases they contain no halogen at all (4,5).

The most stable dihalomethylene should have the longest existence and might be captured in the highest yield. Recent work concerning a halogen's ability to share one of its electron pairs (6,7), and specifically its ability to stabilize a dihalomethylene intermediate (8), indicates that fluorine will participate in resonance of this type better than any of the other halogens. Difluoromethylene has been reported as an intermediate in several gas phase reactions,

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(4) E. L. Pollitzer, A Study of the Reactions of Alkali Metal Alkoxides with Haloforms, Ph.D. Thesis, Georgia Institute of Technology, Atlanta, Georgia, 1953.

(5) J. Hine, A. M. Dowell, Jr., and J. E. Singley, Jr., Journal of The American Chemical Society, 78, 479 (1956).

(6) R. W. Taft, Jr., Ibid., 79, 1045 (1957).

(7) C. K. Ingold, Structure and Mechanism in Organic Chemistry, Cornell University Press, Ithaca, N.Y., 1953, pp. 75-89.

(8) J. Hine and S. J. Ehrenson, Journal of The American Chemical Society, 80, 824 (1958).

a fact that further substantiates its relative stability (9,10,11,12). Since fluorine is usually relatively unreactive in saturated organic compounds, it might be possible to capture the difluoromethylene without the captured product undergoing further reaction and prove the existence of a methylene synthetically.

It has been shown that the haloform deuteriobromodifluoromethane does not undergo deuterium exchange with the solvent but goes directly to the difluoromethylene intermediate (13). One reason for this haloform to avoid carbanion formation is undoubtedly the lack of ability of fluorine to stabilize a carbanion (14). Here the high energy required for fluorine to expand its outer electronic octet would explain why it is the poorest of the halogens at facilitating carbanion formation, despite its high electronegativity.

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(9) J. Dacey and J. Hodgins, Canadian Journal of Research, 28B, 90, 173 (1950).

(10) P. Venkateswarlu, Physical Reviews, 77, 676 (1950).

(11) R. K. Laird, E. B. Andrews and R. F. Barrown, Transactions of The Faraday Society, 46, 803 (1950).

(12) J. L. Margrave and K. Wieland, Journal of Chemical Physics, 21, 1552 (1953); and references cited therein.

(13) J. Hine and P. B. Langford, Journal of The American Chemical Society, 79, 5497 (1957).

(14) J. Hine, N. W. Burske, M. Hine and P. B. Langford, Ibid., 79, 1406 (1957).

Another point of interest is that orthoesters are among the major products in the alcoholic solvolysis of haloforms. If the difluoromethylene intermediate could be captured by a nucleophilic reagent to give as an initial product, a relatively unreactive species, it might be possible to learn whether the orthoesters isolated were formed by attack of the nucleophile on this initial product or by a separate reaction path.

To carry out this research the haloform chlorodifluoromethane was chosen as the most readily available source of difluoromethylene. It was decided to study the reaction of this haloform with sodium methoxide and sodium thiophenoxide with the hope of capturing the difluoromethylene intermediate. The results of these experiments might better explain the mechanism of solvolysis of haloforms containing two fluorine atoms.

CHAPTER II

PROCEDURE

Reaction of Chlorodifluoromethane with Sodium Methoxide (15).--Seventy-two grams (3.1 moles) of sodium was dissolved in about 600 ml. of methanol in a one-liter three-neck flask equipped with a fritted-glass gas-inlet tube and a -80° reflux condenser. Chlorodifluoromethane was then admitted to the flask rapidly causing an exothermic reaction. After 90 minutes the continual return of cold product from the reflux condenser had caused so much cooling that the reaction was proceeding rather slowly. Therefore the admission of haloform was interrupted and after allowing a few minutes for the residual haloform to react and the Dry Ice in the condenser to sublime the reaction flask was heated until methanol began to reflux, the more volatile products being collected in a trap at -80°. The admission of chlorodifluoromethane was resumed until the reaction appeared to be essentially complete and the distillation of volatile material repeated.

During the reaction a large amount of salt had precipitated from the reaction mixture. This was collected on a filter, washed with methanol, dried and found to weigh

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(15) J. Hine and J. J. Porter, Journal of The American Chemical Society, 79, 5493 (1957).

130 g. Titration for chloride (Fajans) and fluoride (16) and for base showed that the material included 87.0 g. (1.49 moles) of sodium chloride and 42.4 g. (1.01 moles) of sodium fluoride and 0.01 mole of base. The methanolic filtrate was fractionally distilled through a 30-inch column packed with glass helices, giving as the only products methanol (containing some trimethyl orthoformate) and pure trimethyl orthoformate (b.p. 98-99.5° at 740 mm.--infrared spectrum identical to that of authentic material). Including the material present in the methanol (analyzed by infrared measurements), 51 g. (0.48 mole) of trimethyl orthoformate was obtained.

The volatile material collected at -80° was distilled through a 2 ft. column packed with glass helices and equipped with condensers through which refrigerated glycol-water was circulated.

The fraction boiling at -4° at 740 mm. occupied 54 ml. at -80°, but it was clear that not all of the material was being condensed by the coolant which was at -8°. The infrared spectrum of this material is shown in Figure 3. This difluoromethyl ether is rather unstable, decomposing on standing to liberate hydrogen fluoride. When about 0.5 ml. of sulfuric acid was added to about 10 ml. of the material refluxing at -4°, there was a slow evolution of gas that was

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(16) I. M. Kolthoff and E. B. Sandell, Textbook of Quantitative Inorganic Analysis, 3rd Ed., The Macmillan Co., New York, N.Y., 1952, p. 721.

not condensed in the -80° reflux condenser. Infrared measurements showed that this gas contained carbon monoxide. The reflux condenser was then removed, the difluoromethyl ether allowed to evaporate and the remaining solution heated to 50° with the evolution of gas. This gas, collected after passage through a short tube filled with sodium hydroxide pellets, had an infrared spectrum identical to that of methyl formate except for a band at 9.75 μ, probably due to silicon tetrafluoride (17).

From data on related compounds the density of difluoromethyl methyl ether at -80° is estimated as 1.10. Thus the yield of this product is 59 g. (0.72 mole) or 48 per cent based on the haloform reacted (sodium chloride formed). Since a 32 per cent yield of trimethyl orthoformate was obtained, 80 per cent of the haloform that reacted was accounted for. From the relative yields of chloride and fluoride a 34 per cent yield of the orthoester and 66 per cent of the difluoromethyl ether would be expected.

Kinetics of the Reaction of Chlorodifluoromethane with Sodium Methoxide at 35°.--To a 250 ml. volumetric flask was added 100 ml. of 0.0930 M chlorodifluoromethane. The flask was then placed in a constant temperature bath and allowed to equilibrate. Twenty-five milliliters of 0.3 M NaOMe, at 35°, was pipetted into the flask which was then filled to the mark

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(17) K. W. F. Kohlrausch, Der Smekal-Raman-Effekt, Ergänzungsband, 1931-1937 (J. Springer, Berlin, 1938).

with methanol at 35°. At intervals of time 25 ml. samples were withdrawn and placed in a flask containing 0.1052 M p-toluenesulfonic acid to stop the reaction and then the excess acid was back-titrated with 0.05116 M sodium hydroxide using p-nitrophenol as an indicator.

To determine f_o, the fraction of orthoester formed in this reaction from equation 1, eight 25 ml. volumetric flasks containing 20 ml. of 0.045 M chlorodifluoromethane were placed in a constant temperature bath at 35°. To each was added 1 ml. of 0.8 M sodium methoxide and sufficient methanol to fill the flask to the mark. At intervals of time the flasks were removed from the bath and the contents emptied into a flask containing 0.1138 M perchloric acid to stop the reaction. The excess acid was back-titrated with 0.0776 M sodium hydroxide using p-nitrophenol as an indicator. The solution was then titrated for chloride content using 0.0480 M silver nitrate (Fajans) (16). These results are shown in Table 7.

Kinetics of the Reaction of Chlorodifluoromethane with Sodium Methoxide and Sodium Thiophenoxide at 35°.--To a 100 ml. volumetric flask was added 25 ml. of 0.555 M chlorodifluoromethane and after half an hour in a constant temperature bath 1.54 ml. of thiophenol was syringed into the flask and 8 ml. of 3.5 M sodium methoxide added. The time was recorded and the flask was filled to the mark with methanol, shaken and placed back in the bath. At intervals

of time 10 ml. samples were withdrawn and placed in a flask containing 0.2226 M hydrochloric acid. The excess hydrochloric acid was back-titrated with 0.0512 M sodium hydroxide using p-nitrophenol as an indicator. To determine the thiophenol concentration the solution was titrated with 0.0269 M methanolic iodine to an iodine color. The first sample was used to determine the initial concentration of sodium methoxide and sodium thiophenoxide. The results of this run are shown in Table 2.

A second run was made in the same manner except that thiophenol was used in excess to give a methoxide-free solution. The results of this run are shown in Table 8.

Reaction of Chlorodifluoromethane with Sodium Methoxide and Sodium Thiophenoxide.--One hundred and eighty-five grams (8.04 moles) of sodium was dissolved in about 1600 ml. of methanol in a two-liter three-neck flask equipped with a stirrer, Dry Ice-cooled reflux condenser and a gas dispersion tube. To the flask was added 168 g. (1.53 moles) of thiophenol with stirring and then chlorodifluoromethane was bubbled into the reaction mixture. The reaction temperature dropped from 64° down to 50° at which time the gas addition was discontinued and the Dry Ice allowed to sublime from the condenser. The flask was then heated to remove the difluoromethyl methyl ether produced in the reaction. When the flask temperature reached 64° the heating was stopped and Dry Ice placed in the condenser and the gas addition continued. After

10 hr. the acidimetric and iodimetric titrations showed that only 0.02 moles of sodium methoxide and 0.05 moles of sodium thiophenoxide remained. At this point the reaction was stopped and the Dry Ice condenser removed. After 800 ml. of methanol was distilled from the reaction mixture, it was poured into 5 liters of water. The insoluble organic layer was taken up in one liter of methylene chloride and washed twice with alkali. The aqueous solution was extracted with two 300 ml. portions of methylene chloride which were combined with the original extract. Methylene chloride was then removed from the organic solution by distillation. Distillation of the residue yielded 153 g. of a material boiling at 74-76° (20 mm.) having an infrared spectrum (shown in Figure 4) identical to difluoromethyl phenyl sulfide isolated and identified by Dr. Hine in a similar run (15). The further distillation over a temperature range of 175° to 196° at a pressure of 1 mm. yielded 40 g. of yellow oil. This oil was thought to contain triphenyl orthothioformate but no pure material could be isolated. Infrared spectrum shown in Fig. 5.

Synthesis of Difluoromethyl 2-Naphthyl Sulfone.--The reaction of 25 g. (0.16 mole) of 2-naphthalenethiol and 0.30 mole of sodium methoxide with chlorodifluoromethane in 500 ml. of methanol was carried out using the same apparatus and procedure outlined above for the reaction of sodium thiophenoxide and sodium methoxide with chlorodifluoromethane. After the reaction was assumed to be complete the mixture was poured

into 500 ml. of n-pentane and extracted with two 200 ml. portions of one molar sodium methoxide and then with two 200 ml. portions of water to remove any methanol and dried with Drierite. The n-pentane was removed using a water aspirator leaving about 8.0 ml. of a thick oil.

About two milliliters of the oil was placed in a 50 ml. flask with 10 ml. of glacial acetic acid. The flask was fitted with a reflux condenser and heated to 105°. Then 5.0 ml. of 90 per cent hydrogen peroxide was added slowly to the solution. After all of the hydrogen peroxide was added to the solution it was allowed to reflux for two hours. The solution was then cooled and poured into 50 ml. of water. One methanolic recrystallization of the solid obtained yielded 1.5 g. of white crystals melting at 57.2-58.0°. This material was believed to be difluoromethyl 2-naphthyl sulfone and its infrared spectrum is shown in Figure 6.

Analysis calculated for $C_{11}H_8F_2S$: C, 54.54; H, 3.31; F, 15.70; S, 13.22. Found: C, 54.83, 54.78; H, 3.45, 3.60; F, 15.68, 15.69; S, 12.96, 12.71.[1]

Reactivity of Difluoromethyl Phenyl Sulfide Toward Sodium Methoxide and Sodium Thiophenoxide.--To a 250 ml. volumetric flask was added 100 ml. of a solution 1.8 M in sodium methoxide and 2.2 M in sodium thiophenoxide. The flask was placed in a constant temperature bath at 50°. After half an hour 20.50 g. (0.128 mole) of difluoromethyl phenyl sulfide was

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[1]All analyses were done by Clark Microanalytical Laboratory, Urbana, Illinois.

added to the flask which was then filled to the mark with methanol at 50° and the time recorded. The flask was shaken and placed back in the bath. Twenty milliliter samples were withdrawn at time intervals and titrated with standard 1.3623 M hydrochloric acid using p-nitrophenol indicator and then titrated with 0.5674 M methanolic iodine solution to the color of iodine. The results are shown in Table 19.

Determination of the Acidity of Methanethiol Toward Methanol.-- To determine the acidity of methanethiol relative to methanol, thymol blue (18) was used as an indicator. The basic form of the indicator had a maximum at 5850 Å, at which the neutral form showed negligible absorption. Solutions were made up containing various amounts of 1 M methanolic sodium perchlorate (which showed no effect on the absorption of the indicator), standard sodium methoxide, and standard indicator solution to obtain values for the indicator constants over the desired ionic strength range. The indicator constants calculated from these solutions indicated that an acidic impurity might be present. The values obtained for the indicator constants at approximately the same ionic strength, but different methoxide concentrations, differed by an amount greater than that attributed to experimental procedure. If the indicator constants were calculated assuming a 8×10^{-4} equivalents of acid impurity per mole of sodium perchlorate

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(18) I. M. Kolthoff and L. S. Guss, Journal of The American Chemical Society, 60, 2516 (1938).

used and a 6×10^{-4} N acidic impurity in the methanol we got good agreement for the indicator constants at the same ionic strength. Fifty milliliters of 1 M aqueous sodium perchlorate solution was later found to require 3.5 ml. more 0.003 M sodium hydroxide to raise the pH of the solution to 9.5 than the same volume of water. While this titration was not accurate, it showed that the value we used was reasonable. The assumption that an acid impurity was in the methanol was not verified, but the alcohol had been distilled under air and could have absorbed carbon dioxide. A plot of the logarithm of the indicator constants versus ionic strength is shown in Figure 1 and the data in Table 20.

Measurements on analogous solutions containing known concentrations of methanethiol gave values for the equilibrium constants over the same ionic strength range. A plot of the logarithm of the equilibrium constants versus ionic strength is shown in Figure 2 and the data in Tables 21 and 22.

Reaction of Chlorodifluoromethane with Sodium Methoxide and Sodium Thiomethoxide.--A solution of 1500 ml. of 4.8 M sodium methoxide in methanol was prepared in a three-neck flask with a stirrer and Dry Ice-cooled condenser and 55 g. (1.15 moles) of methanethiol was added. Chlorodifluoromethane was then bubbled into the solution causing the temperature to rise to about 60° but then to fall as the cold difluoromethyl methyl ether (b.p. -5) dripped back into the flask. On four occasions the addition of haloform was interrupted and some of the difluoromethyl methyl ether permitted to distill into a

cold trap. After seven hours of reaction time a sample withdrawn from the reaction mixture was found to be only 0.1 M in total base and so the addition of haloform was stopped; 350 ml. of 7 M sodium methoxide was added to react with any remaining haloform and to prevent the distillation of any methanethiol present. The material in the cold trap was added to the flask whose contents were then fractionally distilled. The 110 ml. of material boiling between -5 and 20° (largely between -5 and 5°) was assumed to be mostly difluoromethyl methyl ether. The 45 ml. collected between 20° and 64° was refractionated to give 2 g., b.p. 28-40°, 2.3 g., b.p. 40-41.1° and 24.5 g., b.p. 41.1-41.5 , $n_D^{20.8}$ 1.3723, $d_4^{20.8}$ 1.1339. From its boiling point, molecular refraction (calcd. 19.20, found 19.66) (19), method of preparation, infrared spectrum (shown in Figure 7) and analysis, it is believed that this material is difluoromethyl methyl sulfide.

Analysis calculated for $C_2H_4F_2S$: C, 24.48; H, 4.11; F, 38.73; S, 32.68. Found: C, 25.47; H, 4.48; F, 8.63, 40.34, 39.87; S, 30.43.

The methanol was largely removed from the remainder of the reaction mixture by fractional distillation and 1200 ml. of petroleum ether was added to the residue. The residue was filtered to remove the salts, which were washed with more petroleum ether. The hydrocarbons were distilled from the

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(19) N. A. Lange, Handbook of Chemistry, 6th Ed., McGraw-Hill Book Co., Inc., New York, N.Y., 1946, p. 1025.

combined organic phase, which was then fractionated in vacuum, to give 4.42 g. boiling point up to 40° (12 mm.), 4.2 g. b.p. 40° (12 mm.), 2.2 g. b.p. 40-89° (12-7 mm.), and 8.2 g. b.p. 89° (7 mm.).

The second fraction, n_D^{24} 1.4510, d_4^{24} 1.0234, is believed to be trimethyl orthomonothioformate, molecular refraction calculated 31.93, found 32.10 (19).

Analysis calculated for $C_4H_{10}O_2S$: C, 39.32; H, 8.25; S, 26.24. Found: C, 39.51, 39.44; H, 7.79, 7.80; S, 26.75, 26.71.

The fourth fraction, m.p. 15.5-16.0 , $n_D^{28.5}$ 1.5670, $d_4^{28.5}$ 1.1309, molecular refraction calculated 44.48, found, 44.48, was found to have an infrared spectrum (shown in Figure 8) identical to that of trimethyl orthothioformate prepared from formic acid and methanethiol by the method of Houben and Schultze (20), who reported a m.p. of 16° and a b.p. of 96° (7 mm.).

Iodimetric titrations showed that 0.57 mole of methanethiol had reacted so that the yields of difluoromethyl methyl sulfide (48%), trimethyl orthothioformate (28%) and trimethyl orthomonothioformate (6%) accounted for 82 per cent of the methanethiol that reacted.

Kinetics of the Reaction of Chlorodifluoromethane with Sodium Methoxide and Sodium Thiomethoxide at 35°.--Two kinetic runs were made in 100 ml. volumetric flasks. Forty milliliters

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(20) J. Houben and K. M. L. Schultze, Berichte der deutschen chemischen Gesellschaft, 44, 3235 (1911).

of 0.3754 M methanolic chlorodifluoromethane solution was pipetted into each flask, which was then placed in a constant temperature bath and allowed to equilibrate. To one flask 40 ml. of a 35° solution, 1.07 M in sodium methoxide and 0.5 M in sodium thiomethoxide was added. The flask was filled to the mark with methanol at 35°, the time was recorded and the flask shaken and placed back in the bath. To the other flask 50 ml. of a solution 1.0 M in sodium thiomethoxide and 0.3 M in methanethiol was added using the same procedure. At intervals of time 10 ml. samples were pipetted from the volumetric flasks into cold Erlenmeyer flasks. The Erlenmeyer flasks were then placed in a beaker of ice water and first titrated with 1.036 N sulfuric acid using p-nitrophenol indicator and then titrated with 0.2500 M methanolic iodine using the color of iodine for the end point. The results are shown in Table 3 and Table 4.

Reactivity of Difluoromethyl Methyl Sulfide Toward Sodium Methoxide and Sodium Thiomethoxide.--Two grams of sodium was dissolved in 50 ml. of methanol in a volumetric flask. After the sodium dissolved about two grams of methanethiol was added to the flask. The flask was placed in a constant temperature bath at 50°. After half an hour 2.00 ml. (0.023 mole) of difluoromethyl methyl sulfide was added to the flask which was then filled to the mark with methanol at 50° and the time recorded. The flask was shaken and placed back in the bath. Ten milliliter samples were withdrawn at time intervals and titrated with standard 1.036 N sulfuric acid

using p-nitrophenol indicator and then titrated with 0.05 M methanolic iodine solution to the color of iodine. The results are shown in Table 11.

Oxidation of Difluoromethyl Phenyl Sulfide to Difluoromethyl Phenyl Sulfone.--The tendency of difluoromethyl phenyl sulfide to become cloudy, then red, with the liberation of hydrogen fluoride, in the absence of added sodium carbonate, caused us to transform it to the more stable sulfone as follows: About 14 g. (0.4 mole) of 90 per cent hydrogen peroxide was dropped into a solution containing 21.5 g. (0.13 mole) of difluoromethyl phenyl sulfide and 60 g. of glacial acetic acid at about 105°. After slow addition of the hydrogen peroxide over a four hour period, most of the acetic acid was removed by distillation. The remainder of the reaction mixture was poured into water and the organic layer taken up in ether, washed with alkali and dried with Drierite. The ether was evaporated and the residue distilled at 7 mm. From the residue was isolated 15.0 g. of material boiling at 115-120°, n_D^{25} 1.4996, d_4^{25} 1.3819, m.p. 24.7-25.0°. The molecular refraction of this compound was calculated using the values listed in Lange's Handbook (19), and an average value of 8.49 ± 0.02 for the $-SO_2-$ group calculated from three cyclic sulfones reported by Grishkevich-Trokhimovskii (21). The value calculated was 39.21, found 40.88. The

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(21) E. Grishkevich-Trokhimovskii, Journal of The Russian Physical Chemistry Society, 48, 880,901 (1916).

infrared spectrum of this sulfone is shown in Figure 9.

Analysis calculated for $C_7H_6O_2SF_2$: C, 43.70; H, 3.12; S, 16.66; F, 19.90. Found: C, 42.91; H, 3.24; S, 15.84, 16.99, 17.03; F, 22.11, 20.08, 20.36.

Reaction of Difluoromethyl Phenyl Sulfone with Sodium Methoxide.--Six grams of difluoromethyl phenyl sulfone was placed in a 50 ml. flask along with 35 ml. of 4.4 M sodium methoxide solution. The flask was fitted with a water cooled condenser and a Dry Ice trap was attached to the outlet of the condenser. The solution was boiled for 5 hr. and then allowed to cool. The infrared spectrum of the material caught in the Dry Ice trap (1-2 ml.) showed it to be essentially pure difluoromethyl methyl ether.

The material in the flask was poured into 200 ml. of water and a 40 ml. sample containing mostly methanol was distilled from the flask. The remaining solution was extracted with 50 ml. of ether and the ether extract discarded. The solution was then made strongly acidic with concentrated hydrochloric acid and extracted with 100 ml. of ether. The ether extract was evaporated to dryness and the remaining solid was taken up in water at 80°. The solution was allowed to stand overnight in a refrigerator and then filtered. The crystals obtained were washed with water and dried overnight in an evacuated desiccator, giving about 1 g. of material melting at 82.7-83.7°. This material was believed to be benzenesulfinic acid (lit. value 83-84° for

melting point (22)).

Kinetics of the Reaction of Difluoromethyl Phenyl Sulfone with Sodium Methoxide at 50°.--Twenty milliliters of a one molar solution of sodium methoxide was pipetted into a 100 ml. volumetric flask along with 60 ml. of methanol. The flask was placed in a constant temperature bath and allowed to equilibrate 30 min. Two milliliters of difluoromethyl phenyl sulfone was added with a syringe and the time recorded. The flask was filled with methanol, shaken and placed back in the bath. At intervals of time 10 ml. samples were removed and titrated with 0.2195 M hydrochloric acid using p-nitrophenol indicator. The results of this run are shown in Table 5.

An additional run was made with a larger excess of sodium methoxide to difluoromethyl phenyl sulfone to determine the ratio of base used per mole of difluoromethyl phenyl sulfone reacting. The results of this run are shown in Table 13.

Kinetics of the Reaction of Difluoromethyl Phenyl Sulfone with Sodium Methoxide and Sodium Thiophenoxide at 50°.--The procedure here was the same as that used for the kinetics of difluoromethyl phenyl sulfone with sodium methoxide alone, except that thiophenol was added. The sodium benzenesulfinate formed in the reaction interfered with the iodine titration

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(22) E. Knoevenagel and J. Kenner, Berichte der deutschen chemischen Gesellschaft, 41, 3315 (1908).

of thiophenol. It was found that thiophenol could be titrated quantitatively with standard sodium hydroxide using the yellow to blue color change of thymol blue for the end point. When samples were removed from the kinetic run, they were first titrated with 0.2195 M hydrochloric acid using p-nitrophenol indicator. This converted all of the sodium thiophenoxide to thiophenol. A few drops of methanolic thymol blue were added and the solution titrated with 0.297 M sodium hydroxide until the blue color of thymol blue appeared. The results of this run and an additional run with excess thiophenol are shown in Table 6 and Table 12.

Reaction of Difluoromethyl Phenyl Sulfone with Sodium Methoxide and Sodium Thiophenoxide.--Twelve grams (0.53 mole) of sodium was dissolved in 300 ml. of methanol in a 500 ml. three-neck flask fitted with a stirrer, thermometer and a water-cooled reflux condenser with the outlet attached to a Dry Ice trap. Twenty-three grams (0.21 mole) of thiophenol and 26.5 g. (0.138 mole) of difluoromethyl phenyl sulfone were added to the flask which was heated to about 50° for 24 hours and then 64° for an additional 24 hr. At this time the reaction was stopped and a sample titrated acidimetrically using standard acid with p-nitrophenol indicator and then back-titrated with standard base to the yellow-to-blue color change of thymol blue. There remained 0.16 mole of sodium methoxide and 0.15 mole of sodium thiophenoxide unreacted.

In the Dry Ice trap was isolated over 4 ml. of a material having an infrared spectrum identical to the

difluoromethyl methyl ether isolated and identified in earlier reactions. If the density of this material is estimated as 1.10 at -80° this corresponds to 4.4 g. (0.054 mole) of difluoromethyl methyl ether or a 39 per cent yield based on the starting difluoromethyl phenyl sulfone.

One hundred and seventy milliliters of methanol was distilled from the reaction flask and the concentrated solution poured into 400 ml. of water. The aqueous solution was extracted with two 200 ml. portions of ether and the ether extracts combined. The ether extract was then distilled and at 65° (10 mm.) 4.98 g. (22 per cent) of difluoromethyl phenyl sulfide (identified by its infrared spectrum) was obtained.

To remove the unreacted thiophenol, the aqueous layer was acidified with 6 M hydrochloric acid to a pH of 5.0, using a Beckman pH meter and extracted with two 300 ml. portions of ether. The aqueous solution was then acidified to a pH of 0.5 and cooled in a refrigerator overnight. Some white crystals were filtered, washed and dried in a desiccator at 1 mm. pressure overnight. These crystals had a melting point of 81.5-82.5° and weighed 2.50 g. A 0.2145 g. sample of this material required 50.5 ml. of 0.0297 M sodium hydroxide for neutralization using p-nitrophenol indicator. This corresponds to a neutralization equivalent of 143. This material was believed to be benzenesulfinic acid, neutralization equivalent 142, m.p. 83-84° (22). The mother liquor was extracted with 200 ml. of ether and the ether removed

from the extract using a water aspirator. This yielded 7.8 g. of a white solid that melted at 72-74° after having been dried overnight in an evacuated desiccator. The combined weight of the two crops of crystals obtained corresponds to a 52 per cent yield of benzenesulfinic acid based on the starting difluoromethyl phenyl sulfone.

Determination of the Extinction Coefficients of Deuteriodifluoromethyl Phenyl Sulfone and Difluoromethyl Phenyl Sulfone in Carbon Disulfide.--A sample of the sulfone, about 0.1 g., was accurately weighed into a tared 10 ml. flask with a ground glass stopper. Then a two ml. sample of carbon disulfide was accurately weighed into the flask and the solution swirled. A portion of this solution was then syringed into a 0.025 mm. sodium chloride infrared cell. Using a scale of 40 inches per micron, resolution of 980, pen response of 2:1, automatic suppression of eight, gain of five, and a speed of three, the extinction coefficients were determined for five absorption peaks for the deuteriated and undeuteriated compounds (deuteriosulfone spectrum in Fig. 10).

The averages of three determinations for each of the extinction coefficients are shown in Table 15. The minimum deuterium content of the sulfone was based on the weakest deuteriodifluoromethyl phenyl sulfone absorption peak. At 12.093μ, where E_H = 1.0106 and E_D = 0.1717 for the 0.025 mm. infrared cell, a value of 0.019 was obtained for the optical density for a 0.1117 M deuterio-sulfone solution. If this absorption was assumed to be due only to the protium compound

it corresponds to 17 per cent difluoromethyl phenyl sulfone.

Kinetics of the Deuterium Exchange of Deuteriodifluoromethyl Phenyl Sulfone with Methanol at 0°.--Fifteen milliliters of 0.079 M sodium methoxide was pipetted into a 50 ml. volumetric flask which was placed in an ice-water bath and allowed to equilibrate. Following this, 0.50 ml. of deuteriated compound was syringed into the flask, which was then filled with methanol at 0°. The flask was shaken and the time recorded. At intervals of time 10 ml. samples were pipetted into 70 ml. of 0.2 M hydrochloric acid and extracted with 1.5 ml. of carbon disulfide. The carbon disulfide extracts were dried with a few pieces of silica gel and then the infrared absorption measured to determine the concentrations of protiated and deuteriated sulfone.

An additional run was made using 45 ml. of 0.079 M sodium methoxide in the same procedure as above. The results of these two runs are shown in Table 15 and Table 16.

Kinetics of the Deuterium Exchange of Deuteriodifluoromethyl Phenyl Sulfone with Water at 0°.--Four hundred milliliters of distilled water and 0.45 ml. of deuteriated sulfone were placed in a 500 ml. volumetric flask and shaken well. The flask was then equilibrated in an ice-water bath. Fifteen milliliters of 0.0297 M sodium hydroxide at 0° was added, the time recorded and the flask shaken and placed back in the ice-water bath. At intervals of time 100 ml. samples were pipetted into a separate flask containing 10 ml. of 0.5 M hydrochloric acid to stop the reaction. The solutions were

then extracted with 1.0 ml. portions of carbon disulfide. The carbon disulfide extracts were dried with a few pieces of silica gel and then the infrared absorption measured to determine the extent of deuterium exchange. An additional run was made using 20 ml. of 0.297 M sodium methoxide using the same procedure as above. The results of these two runs are shown in Table 17 and Table 18.

Reagents.--All methanol was purified by Fieser's (23) method using magnesium. The chlorodifluoromethane used was obtained from Matheson Chemical Company and contained less than 2 per cent dichlorofluoromethane by infrared analysis. The thiophenol, Eastman white label, was used without further purification. Methanethiol was used directly from a lecture bottle obtained from the Matheson Chemical Company. Sodium and carbon disulfide were Baker's reagent grade chemicals. The indicators p-nitrophenol and thymol blue were both Eastman white label chemicals.

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(23) L. F. Fieser, Experiments in Organic Chemistry, 3rd Ed., D. C. Heath and Co., Boston, 1955, p. 289.

CHAPTER III

RESULTS

The Reaction of Chlorodifluoromethane with Sodium Methoxide (15).--The only organic products observed in the reaction of chlorodifluoromethane and sodium methoxide in methanol were methyl orthoformate and difluoromethyl methyl ether. Although the difluoromethyl ether, a new compound, was not analyzed because of its tendency to decompose on standing, the following evidence exists for its structure. Its method of preparation is analogous to that used for difluoromethyl ethyl ether (24) and difluoromethyl isopropyl ether (25). A survey of twenty-seven series of methyl, ethyl and isopropyl compounds (19) showed that the difference in boiling point between the methyl and ethyl compounds was 3.0 to 12.9° (av. 8.7 ± 2.6) greater than between the ethyl and isopropyl compounds. In view of this the boiling point of difluoromethyl methyl ether (-4°) is quite plausible considering the values reported for the ethyl (23.7°) and isopropyl (44.5°) analogs. Since an alkoxy substituent is known to activate a $-CF_2-$ group so that its acid hydrolysis to a carbonyl group

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(24) A. L. Henne and M. A. Smook, Journal of The American Chemical Society, 79, 5493 (1957).

(25) J. Hine and K. Tanabe, Ibid., 79, 2654 (1957).

occurs readily (24), we carried out the sulfuric acid-catalyzed hydrolysis of our material and identified methyl formate as a reaction product.

$$HCF_2OCH_3 \xrightarrow{H_2SO_4} HCO_2CH_3$$

Our structural assignment is also supported by the infrared spectrum of the compound and by stoichiometric considerations.

The methyl orthoformate and difluoromethyl methyl ether isolated accounted for 80 per cent of the haloform that reacted (as measured by the amount of sodium chloride formed) in a synthetic experiment despite the fact that some of the volatile ether was undoubtedly lost. Assuming these are the only organic products, their relative yields may be calculated from the concentrations of methoxide ion used up and of chloride ion formed. Thus

$$f_o = \frac{(MeO^-)}{2(Cl^-)} - \frac{1}{2} \qquad (1)$$

where f_o is the fraction of the reacted haloform that gave methyl orthoformate. The analogous fraction in the reaction of potassium isopropoxide with chlorodifluoromethane was found to increase somewhat with increasing alkoxide ion concentration (25). This apparently is true in the present case since a much higher fraction of methyl orthoformate was produced in the synthetic run, using concentrated sodium methoxide, than in the kinetic runs. Nevertheless, it was

found that f_o does not change greatly during a kinetic run at the reactant concentrations we used. Assuming f_o constant, the following kinetic equation may be derived.

$$k = \frac{2.303}{t\,[a(1 + 2f_o) - b]} \log \frac{b(a - x)}{a\,[b - (1 + 2f_o)\,x]} \qquad (2)$$

where $a = (CHClF_2)_o$, $b = (MeO^-)_o$, $x = \Delta(CHClF_2)_t$, t = time and k is expressed in l. mole^{-1} (of haloform) sec.$^{-1}$. Typical kinetic data calculated from this equation are shown in Table 1. The fall in rate constants with time probably is due to the loss of the volatile haloform (b.p. -40°) from the reaction solution, so that perhaps the value should be estimated

Table 1. Reaction of Chlorodifluoromethane with Sodium Methoxide in Methanol at 35.0°.[a]

Reaction Time, (sec.)	MeO^- (mole/l.)	10^4 k, l. mole^{-1} sec.$^{-1}$
0	0.02918	
7,595	.02323	7.58
14,478	.01913	7.84
29,910	.01423	7.08
32,270	.01362	7.06
60,945	.00924	6.30
75,802	.00707	6.60
	Av.	7.09 ± 0.41

[a] $(CHClF_2)_o$ = 0.03721 M. The value used for f_o was 0.075 and was taken from the data shown in Table 7.

as about 7.8 x 10^{-4}, by extrapolation to zero time.

Reaction of Chlorodifluoromethane with Sodium Methoxide and Sodium Thiophenoxide.--In the reaction of chlorodifluoromethane with sodium methoxide and sodium thiophenoxide difluoromethyl phenyl sulfide was isolated in addition to the products already found in the absence of sodium thiophenoxide. Triphenyl orthothioformate was also believed to be present as a small amount of material (1.5-2 g.) having a melting point of 37-40°(reported (26), 39.5°) was isolated. This product could not have come from the reaction of difluoromethyl phenyl sulfide which was found to be stable to the reaction conditions. In one run difluoromethyl phenyl sulfide was isolated in more than 60 per cent yield, based on the thiophenoxide reacting.

We have made a quantitative estimate of the tendency of the thiophenoxide ion to combine with difluoromethylene as follows. Difluoromethylene might be expected to combine with any of the three nucleophilic reagents, methanol, methoxide ion or thiophenoxide ion. Neglecting that small though significant part of the reaction that proceeds far enough to liberate fluoride ion, we may write

$$CF_2 + CH_3OH \xrightarrow{k_M} CH_3OCHF_2$$

$$CF_2 + CH_3O^- \xrightarrow[CH_3OH]{k_B} CH_3OCHF_2$$

$$CF_2 + C_6H_5S^- \xrightarrow[CH_3OH]{k_T} C_6H_5SCHF_2$$

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(26) S. Gabriel, Berichte der deutschen chemischen Gesellschaft, 10, 185 (1877).

From this reaction scheme (treating k_M as a first-order rate constant) and the assumption that difluoromethylene is formed only by the action of methoxide ion on the haloform, we may express the rate of reaction of thiophenoxide ion

$$\frac{d\,(C_6H_5S^-)}{dt} = k\,(CHClF_2)\,(MeO^-)\left(\frac{k_T\,(C_6H_5S^-)}{k_T\,(C_6H_5S^-) + k_B\,(MeO^-) + k_M}\right) \qquad (3)$$

and the rate of reaction of methoxide ion is expressed

$$\frac{d\,(MeO^-)}{dt} = k\,(CHClF_2)\,(MeO^-)\left(\frac{k_B\,(MeO^-) + k_M}{k_T\,(C_6H_5S^-) + k\ \ (MeO^-) + k_M}\right) \qquad (4)$$

Dividing eq. 2 by eq. 3

$$\frac{d\,(C_6H_5S^-)}{d\,(MeO^-)} = \frac{k_T\,(C_6H_5S^-)}{k_B\,(MeO^-) + k_M} \qquad (5)$$

By the use of both acidimetric and iodimetric titrations the changes in thiophenoxide and methoxide ion concentrations may be determined. We now simplify eq. 4 by neglecting the reaction of difluoromethylene with methoxide ion. This point will be discussed later. With this simplification equation 4 becomes 6 where $T = (C_6H_5S^-)_o$, $y = \Delta\,(C_6H_5S^-)$ and $z = \Delta\,(MeO^-)$.

$$\frac{dy}{dz} = (k_T/k_M)\,(T - y) \qquad (6)$$

Integration of equation 5 yields

$$(k_T/k_M) = \frac{2.303}{z} \log \frac{T}{T - y} \qquad (7)$$

In Table 2 are shown data on a run calculated according to equation 7 which is based on the assumption that thiophenoxide

Table 2. Reaction of Chlorodifluoromethane with Sodium Thiophenoxide and Sodium Methoxide at 35°.[a]

Reaction Time, (sec.)	$C_6H_5S^-$ (mole/l.)	MeO^- (mole/l.)	k_T/k_M
0	0.1509	0.2043	
2,985	.1304	.1722	4.55
8,235	.1153	.1452	4.55
21,885	.1022	.1233	4.81
35,790	.0997	.1040	4.13
70,530	.0970	.1016	4.30
		Av.	4.47 ± 0.20

[a] $(CHClF_2)_o = 0.1388$ M

ion is competing only with the solvent methanol for the intermediate difluoromethylene. If the methoxide ion had been a major competitor, the calculated values of k_T/k_M should increase as the reaction proceeds and the concentration of methoxide ion decreases. For this reason it was originally assumed that the neglect of the methoxide term in equation 5 was justified. In a later study of difluoromethyl phenyl sulfone that will be discussed in this section considerable doubt was cast upon this assumption. Since

methanol is present at a concentration of about 25 M, the values of k_T/k_M found show that the thiophenoxide ion is more than 100 times as reactive.

The Determination of the Acidity of Methanethiol Toward Sodium Methoxide.--For the kinetic study of chlorodifluoromethane with sodium methoxide and sodium thiomethoxide it was necessary to determine the acidity of methanethiol toward sodium methoxide. This would enable us to calculate the concentration of methoxide in a kinetic run and determine its catalytic effect in the reaction of chlorodifluoromethane with sodium thiomethoxide. The equilibrium constant was determined for the following equation:

$$CH_3SH + CH_3O^- \rightleftharpoons CH_3S^- + CH_3OH$$

The work of Kolthoff and Guss (18) showed that thymol blue would be a suitable indicator in this determination. Indicator constants were determined over the ionic strength range 0.2 to 0.55. The indicator constant K_{In} is defined here as the autoprotolysis constant for methanol divided by the second ionization constant of the indicator.

$$K_{MeOH} = (CH_3O^-)(CH_3OH_2^+); \quad K_1 = \frac{(In^=)(CH_3OH_2^+)}{(In^-)}$$

$$K_{In} = \frac{(In^-)(CH_3O^-)}{(In^=)}$$

In^- and $In^=$ represent the two forms of the indicator. The values for K_{In} were determined using the Beckman D. U.

spectrophotometer at known ionic strengths and a logarithmic plot of K_{In} versus ionic strength is shown in Figure 1.

The equilibrium constants defined by the following equation

$$K_e = \frac{(CH_3S^-)}{(CH_3O^-)(CH_3SH)}$$

were then determined over the ionic strength range 0.02 to 0.55 and a plot of log K_e versus ionic strength is shown in Figure 2.

The Reaction of Chlorodifluoromethane with Sodium Methoxide and Sodium Thiomethoxide.--The sulfur-containing products in the reaction of chlorodifluoromethane with sodium methoxide and sodium thiomethoxide were difluoromethyl methyl sulfide, trimethyl orthomonothioformate and trimethyl orthothioformate. These compounds were isolated in 44.2 per cent, 6.1 per cent and 28.2 per cent yields respectively based on the methanethiol that reacted. No attempt was made to isolate the products already found in the earlier reaction of the haloform with sodium methoxide alone.

A kinetic study was carried out on the reaction of chlorodifluoromethane with sodium methoxide and sodium thiomethoxide. It was assumed that the major part of the reaction was initiated by methoxide and therefore only haloform and methoxide would appear in the rate expression. In the kinetic study the ratio of methoxide reacting per mole of haloform was taken to be the difference in the initial and

final methoxide concentration divided by the intial haloform concentration since base was in excess. This ratio is identified as n in the following kinetic equation

$$k = \frac{2.303}{t(an-b)} \log \frac{b(a-x)}{a(b-nx)} \qquad (8)$$

where $a = (CHClF_2)_o$, $b = (MeO^-)_o$, $x = \Delta(CHClF_2)$ at time t, n as defined above, t = time in sec., and k is expressed in l. $mole^{-1}$ (of haloform) $sec.^{-1}$. The results of the kinetic study are shown in Table 3.

To show the catalytic effect of methoxide on the reaction of chlorodifluoromethane with sodium thiomethoxide an additional run was made with a much lower concentration of methoxide. This was done by adding an excess of methanethiol to the solution. In this case the methoxide concentration was found to remain essentially constant throughout the run so a first-order rate expression appeared applicable for the disappearance of haloform. The kinetic equation used was as follows

$$k = \frac{2.303}{t} \log \frac{C_o}{C} \qquad (9)$$

where $C_o = (CHClF_2)_o$ and $C = (CHClF_2)_t$, t in seconds and k expressed in $sec.^{-1}$. The concentration of haloform that had reacted by a given time was set equal to the change in methoxide plus thiomethoxide concentrations divided by 1.1. This is a ratio of total base reacting per mole of haloform and was calculated from the data in Table 3 where the

Table 3. Reaction of Chlorodifluoromethane with Sodium Methoxide and Sodium Thiomethoxide at 34.5°.

Reaction Time, (sec.)	MeS^- (mole/l.)	MeO^- (mole/l.)	10^4 k, l. $mole^{-1}$ $sec.^{-1}$
0	0.1976[a]	0.2290[a]	
120	.2005	.2191	
1,650	.1768	.2065	7.21
5,520	.1525	.1666	9.43
9,520	.1461	.1440	12.01
28,440	.1312	.1299[b]	
89,920	.1254	.1336	
		Av.	9.55 ± 1.64

[a]All methoxide and thiomethoxide concentrations were calculated using the data in Table 9 and a value of 264 for the equilibrium constant K_e taken from Figure 2. $(CHClF_2)_o$ = 0.1502 M.

[b]The value of n was calculated from the difference (0.2290 - 0.1299) in methoxide ion concentration divided by the initial haloform concentration (0.1502) and was assumed constant throughout the run. The reaction was assumed complete at 28440 seconds.

reaction was assumed complete. It is in agreement with the values obtained for the haloform with methoxide alone. The results of this kinetic study are shown in Table 4.

In connection with the synthetic work it was necessary to determine the reactivity of difluoromethyl methyl sulfide under the reaction conditions. This compound was found to be less than 6 per cent reacted after having been exposed to 0.77 M sodium methoxide and 0.46 M sodium thiomethoxide at 50° for 22 days. The results of this reaction are shown in Table 11.

Table 4. Reaction of Chlorodifluoromethane with Sodium Thiomethoxide and Excess Methanethiol at 34.5°.

Reaction Time, (sec.)	MeS^- (mole/l.)	MeO^- (mole/l.)	10^6 k, $sec.^{-1}$
0	0.5019[a]	0.0101[a]	
120	.4952	.0104	
2,310	.4872	.0101	
22,860	.4546	.0095	12.7
26,460	.4488	.0091	12.8
66,480	.4147	.0101	10.1
157,200	.3754	.0090	8.4
	Av.	.0097	11.4 ± 1.7

[a]All methoxide and thiomethoxide concentrations were calculated using the data in Table 10 and a value of 321 for the equilibrium constant K_e taken from Figure 2. $(CHClF_2)_o$ = 0.1502 M.

The Reaction of Difluoromethyl Phenyl Sulfone with Sodium Methoxide.--The synthetic reaction of difluoromethyl phenyl sulfone with sodium methoxide yielded a gas shown to be the same difluoromethyl methyl ether that was isolated in the reaction of chlorodifluoromethane with sodium methoxide. The other product isolated was benzenesulfinic acid. This reaction was carried out on a small scale and no yields were determined, but these were the only organic products detected.

For the kinetic study it was necessary to determine the ratio of difluoromethyl phenyl sulfone reacting per mole of sodium methoxide. This ratio was approximated from a value obtained in an additional run in which the methoxide

concentration was in excess (shown in Table 13) and from the ratio obtained in the reaction of chlorodifluoromethane with sodium methoxide (shown in Table 7). While two different reactions were used to calculate this ratio, the same intermediate, which in this case appears to control the ratio, is proposed for both reactions.

Table 5. Reaction of Difluoromethyl Phenyl Sulfone with Sodium Methoxide in Methanol at 50.4°.[a]

Reaction Time, (sec.)	MeO^- (mole/l.)	10^5 k, l. mole^{-1} sec.$^{-1}$
0	0.2360	
27,720	.2019	3.47[b]
70,080	.1670	3.50
85,560	.1580	3.50
108,480	.1455	3.56
155,580	.1253	3.73
	Av.	3.55 ± 0.07

[a]The initial concentration of sulfone was 0.1379 M.

[b]All k's were calculated from equation 8 where a is now defined as initial sulfone concentration, $x = \Delta(C_6H_5SO_2CF_2H)_t$ and n = 1.30.

Hine and Tanabe have shown that the ratio of moles of potassium isopropoxide to moles of chlorodifluoromethane reacting increases with increasing isopropoxide concentration (27). Since our kinetic study was carried out at an

(27) J. Hine and K. Tanabe, Journal of The American Chemical Society, 80, 3002 (1958).

intermediate average sodium methoxide concentration of 0.190 M we chose an intermediate value of 1.30 for the ratio of difluoromethyl phenyl sulfone reacting per mole of sodium methoxide. The results of this kinetic study are shown in Table 5.

The Reaction of Difluoromethyl Phenyl Sulfone with Sodium Methoxide and Sodium Thiophenoxide.--The organic products isolated from a synthetic reaction were difluoromethyl methyl ether in 38 per cent yield, difluoromethyl phenyl sulfide in 22 per cent yield and benzenesulfinic acid in 52 per cent yield, all based on the reacting sulfone. No attempt was made to recover trimethyl orthoformate possibly produced in the reaction but an attempt to isolate triphenyl orthothioformate was unsuccessful.

The kinetic study of this reaction showed that the rate of disappearance of difluoromethyl phenyl sulfone was essentially independent of the thiophenoxide concentration. The results of this study are shown in Table 6 and Table 12. The values of k_T/k_M calculated using equation 7 are also listed in Table 6. The previously described assumption based on the data in Table 2 that methoxide was not a major capturing agent for difluoromethylene may not be valid since the data in Table 6 seem to show that k_T/k_M increases as the reaction proceeds. There are not enough data to reach a definite conclusion about whether methoxide is a major capturing agent; however, whether it is or not the relative values obtained for k_T/k_M in Table 6 and Table 2 should be of significance

Table 6. Reaction of Difluoromethyl Phenyl Sulfone with Sodium Methoxide and Sodium Thiophenoxide at 50.4°.[a]

Reaction Time, (sec.)	$NaSC_6H_5$ (mole/l.)	NaOMe (mole/l.)	10^5 k, l. mole^{-1} sec.$^{-1}$	k_T/k_M[c]
0	0.1871	0.2150		
27,840	.1776	.1962	3.15[b]	2.77
69,960	.1663	.1722	3.50	2.75
86,560	.1580	.1680	3.25	3.60
109,620	.1533	.1621	3.07	3.77
156,480	.1449	.1453	3.35	3.66
		Av.	3.28 ± 0.15	3.29 ± 0.44

[a]The initial concentration of sulfone was 0.1379 M.

[b]The k's were calculated from equation 8 where a is now defined as initial sulfone concentration, t in sec., $x = \Delta(C_6H_5SO_2CF_2H)_t$ and n = 0.829. The value of n for the kinetic equation was taken as the average of the values obtained from each point of this run from the equation

$$n = \frac{\Delta(\text{NaOMe}) \times 1.30}{\Delta(\text{NaOMe}) + \Delta(NaSC_6H_5)}$$

where 1.30 is the value of n used in Table 5 and assumed applicable to this run.

[c]The values of k_T/k_M were calculated using equation 7.

since the methoxide ion concentrations were comparable in the two cases. The smaller value shown in Table 6 may reflect a decrease in selectivity of difluoromethylene resulting from the 15° temperature increase.

The Kinetics of the Base-Catalyzed Deuterium Exchange of Deuteriodifluoromethyl Phenyl Sulfone in Methanol at 0°.--The

rate of deuterium exchange of the deuteriosulfone was measured spectrophotometrically using the Perkin-Elmer Model 21 infrared spectrophotometer. The first-order exchange rate was calculated using the following equation:

$$k = \frac{2.303}{t} \log \frac{100}{D} \qquad (10)$$

where D equals the per cent deuterium compound remaining after time t and k is expressed in $sec.^{-1}$. The per cent deuterium compound was found by solving the following equation at two wave lengths.

$$\text{Optical Density} = E_D C_D + E_H C_H \qquad (11)$$

where E_H and E_D are the extinction coefficients for the protium and deuterium compound at the same wave lengths and C_H and C_D are the corresponding concentrations of the protium and deuterium compounds. The first-order rate constants calculated from two runs with different methoxide concentrations were divided by their corresponding methoxide concentrations to obtain the second-order rate constants. The average value obtained was $9.54 \pm 0.35 \times 10^{-4}$ l. $mole^{-1}$ (of deuteriosulfone) $sec.^{-1}$. The experimental results of these two runs are shown in Table 15 and 16.

The Kinetics of the Base-Catalyzed Deuterium Exchange of Deuteriodifluoromethyl Phenyl Sulfone with Water at 0°.--The rate of exchange was measured spectrophotometrically as in methanol. The procedure for calculating the first-order

exchange rate is the same as that for methanol outlined above. The experimental results for two runs are shown in Table 17 and 18. The average second-order rate constant obtained by dividing the first-order rate constants by their corresponding hydroxide concentrations is $6.00 \pm 0.25 \times 10^{-2}$ l. mole^{-1} (of deuteriosulfone) sec.$^{-1}$.

CHAPTER IV

DISCUSSION AND CONCLUSIONS

Reaction of Chlorodifluoromethane.--It was found that chlorodifluoromethane reacted with base at a rate faster than it would have been predicted to undergo carbanion formation by a correlation described in earlier work (13). This ability for chlorodifluoromethane to by-pass carbanion formation (deuteriobromodifluoromethane has been found not to exchange deuterium but to solvolyze directly to products (13)) is undoubtedly due to the presence of two fluorine atoms in the haloform.

In the haloform series the first two steps of the general solvolysis mechanism are those of initial trihalocarbanion formation followed by loss of a halogen anion to give a dihalomethylene. This mechanism, termed an α-elimination (28), has been found valid for all of the haloforms studied containing no more than one fluorine atom (8). In the case of chlorodifluoromethane it appears that the increase in stability afforded the methylene intermediate by two fluorine atoms has more than offset the destabilization of the would-be carbanion.

The ability of a fluorine to stabilize a dihalomethylene

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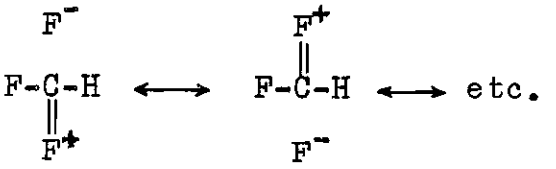
(28) For the meaning of α-elimination see J. Hine, Physical Organic Chemistry, McGraw-Hill Book Co., Inc., New York, N.Y., 1956, Chap. 5, Section 6.

and thus increase the rate of hydrolysis of a haloform while at the same time destabilizing a carbanion and decreasing the rate of carbanion formation has been explained by Hine and Ehrenson (8). Fluorine, being a first row element, would be expected to enter into electron donating resonance with carbon much better than the other halogens (29), but not having available d-orbitals it could not accept an electron pair and stabilize a carbanion. Burske found that fluoroform did not react with potassium t-amyloxide after treatment for several days at 50° (30). The lack of solvolysis of fluoroform is probably due to no-bond resonance stabilization by fluorine. This type of resonance has been used to explain the observed C-F bond shortening in halogens containing at least two fluorine atoms (31) as compared to the C-F bond length in fluoromethane. The structures of the following type



would explain the added stability and greater bond shortening

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(29) For a discussion of this see J. Hine, Physical Organic Chemistry, Chap. 2 and 6.

(30) N. W. Burske, The Kinetics of the Catalyzed Deuterium Exchange of Some Haloforms in Aqueous Solution, Ph.D. Thesis, Georgia Institute of Technology, Atlanta, Georgia, 1957, p. 11.

(31) L. O. Brockway, Journal of Physical Chemistry, 41, 187 (1937).

in fluoroform as compared to the other haloforms. This type of resonance stabilization would be lost in the trifluorocarbanion, as it would require placing negative charges on adjacent atoms. The trifluorocarbanion has been shown to exist, however, in the decomposition of trifluoroacetic acid (32). Verhoek and coworkers postulated its existence in the decarboxylation carried out at 170-200° in ethylene glycol. This high temperature required for decarboxylation is no doubt due to the presence of the three fluorine atoms, as chlorodifluoroacetic acid has been shown to decarboxylate at much lower temperatures (33).

The products isolated from the reaction of chlorodifluoromethane with sodium methoxide in methanol, difluoromethyl methyl ether (48 per cent) and methyl orthoformate (32 per cent) accounted for 80 per cent of the haloform reacting. The mechanism proposed for their formation is as follows:

$$CHClF_2 + CH_3O^- \xrightarrow{CH_3OH} CF_2$$

$$CF_2 \xrightarrow{CH_3OH} CH_3OCF_2H$$

$$CF_2 \xrightarrow{CH_3OH} CH_3O\text{-}C\text{-}F$$

$$CH_3O\text{-}C\text{-}F \xrightarrow{CH_3OH} (CH_3O)_3CH$$

The kinetic study showed that the number of moles of

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(32) I. Auerbach, F. H. Verhoek, and A. L. Henne, Journal of The American Chemical Society, 72, 299 (1950).

(33) J. Hine and D. C. Duffy, Ibid., 81, 1131 (1959).

base reacting per mole of haloform remained essentially constant throughout the reaction and therefore the methyl orthoformate produced must not be formed from difluoromethyl methyl ether. If the orthoformate had been formed by attack on the difluoromethyl methyl ether the ratio of base to haloform reacted would have increased as the reaction progressed. The most reasonable mechanism leading to methyl orthoformate is through a fluoromethoxymethylene as shown above.

In order to obtain additional evidence for the concerted α-elimination mechanism shown above sodium thiophenoxide was used. If a difluoromethylene was being formed as an intermediate, it would be expected to be subject to nucleophilic attack since it has an electron-deficient carbon atom. The thiophenoxide ion was previously found to be effective at capturing other dihalomethylenes (5) and therefore should be suitable for this case. The reaction of sodium thiophenoxide with chlorodifluoromethane was studied and found to be a very slow process at 35° in methanol, the second-order rate constant being about 5×10^{-6} l. mole^{-1} sec.$^{-1}$. This low reactivity of the haloform toward such a strongly nucleophilic reagent is itself evidence that the 150-fold faster reaction with methoxide ion (the second-order rate constant for reaction with methoxide is 7.09×10^{-4} l. mole^{-1} sec.$^{-1}$) is not S_N2 in character since in other S_N2 reactions the thiophenoxide ion has been found to be from twenty to ten thousand (34)

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(34) J. Hine, S. J. Ehrenson and W. H. Brader, Jr., Journal of The American Chemical Society, 78, 2282 (1956).

times as reactive as the methoxide ion.

The product isolated from the reaction of chlorodifluoromethane with sodium methoxide and sodium thiophenoxide was difluoromethyl phenyl sulfide. This product accounted for more than 60 per cent of the thiophenoxide ion reacting and was found to be stable to the reaction conditions. The presence of two fluorine atoms on the same carbon atom appears to change the reactivity considerably as judged by comparing α-fluoroalkyl halides, which are the most reactive of the monohaloalkyl halides in nucleophilic displacement reactions (35), to the difluoromethyl phenyl sulfide we isolated.

In the base-catalyzed reaction of chloroform with sodium thiophenoxide the only sulfur-containing product isolated was triphenyl orthothioformate (1). The initial reaction product of the intermediate dichloromethylene with thiophenoxide ion must be considerably more reactive than the intermediate difluoromethylene reaction product we captured as no chlorine-containing product was isolated. This is not surprising in view of the relative reactivities of dichloromethyl methyl and difluoromethyl methyl ether. Rosscup calculated a value of 1.26×10^{-2} l. mole^{-1} sec.$^{-1}$ for the rate constant for the reaction of dichloromethyl methyl ether with

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(35) J. Hine, C. H. Thomas and S. J. Ehrenson, Journal of The American Chemical Society, 77, 3886 (1955).

potassium isopropoxide at -12° (36). While we did not calculate a rate constant for the reaction of difluoromethyl methyl ether with sodium methoxide, we did isolate the difluoromethyl ether from a reaction carried out for 8 hours at a temperature of over 50°. The stability of difluoromethyl phenyl sulfide led us to believe that the unidentified high-boiling fraction contained products formed from an additional reaction path.

An additional reaction was carried out using sodium thiomethoxide as the capturing agent for the difluoromethylene intermediate to obtain lower-boiling products. The products obtained from the reaction of chlorodifluoromethane with sodium methoxide and sodium thiomethoxide were difluoromethyl methyl sulfide, trimethyl orthomonothioformate and trimethyl orthothioformate. In order to learn more about the mechanism of the formation of these compounds kinetic studies were carried out on the reaction. The greater basicity of thiomethoxide compared to the thiophenoxide used in the preceding case made it necessary to determine an equilibrium constant for the following equation

$$CH_3SH + CH_3O^- \rightleftharpoons CH_3S^- + CH_3OH$$

in order to know the methoxide concentration in a kinetic run. While the reaction of thiophenol with sodium methoxide

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(36) R. J. Rosscup, Reactivity and Reaction Mechanisms of Methoxy Chlorides, Ph.D. Thesis, Georgia Institute of Technology, Atlanta, Georgia, 1960.

goes to effective completion it was found that the reaction of methanethiol with sodium methoxide was not complete, having an equilibrium constant of about 100 to 350 over the ionic strength range of 0.2 to 0.5 at 25°.

Measurements were made on two kinetic runs, one in which more sodium methoxide had been added than would be required (stoichiometrically) to transform all of the methanethiol to its salt and the other in which the methanethiol was present in excess. Data on the two runs are given in Table 3 and 4. The reaction rate was assumed to be dependent only on the concentrations of chlorodifluoromethane and methoxide. The second-order rate constant obtained from the run with sodium methoxide in excess was 9.55×10^{-4} l. mole^{-1} sec.$^{-1}$. In the second run, in which methanethiol was in excess, the equilibrium concentration of methoxide remained essentially constant throughout the run. This reduced the reaction to a first-order process with the rate being dependent only on the chlorodifluoromethane concentration. The second-order rate constant was obtained by dividing the first-order constant by the average methoxide concentration throughout the run. The value obtained was $11.3 \pm 1.7 \times 10^{-4}$ l. mole^{-1} sec.$^{-1}$. The rate constant obtained in the run with excess methoxide in which the ratio of $(MeS^-)/(MeO^-)$ was near unity and in the run with excess methanethiol in which the ratio $(MeS^-)/(MeO^-)$ was about 45 shows that the reaction of chlorodifluoromethane with thiomethoxide contributes very little to the reaction rate.

Part of the increase in rate between the first run where the ionic strength was about 0.42 M and the second, in which the ionic strength was about 0.50 M, may be an ionic strength effect since the second-order rate constant for the reaction of methoxide ions with chlorodifluoromethane was found to be 7.09×10^{-4} l. $mole^{-1}$ $sec.^{-1}$ at 35° at an ionic strength of 0.03 M. If the entire increase is due to added α-elimination by thiomethoxide then 15 per cent of the reaction containing excess methanethiol must be due to thiomethoxide ion. Considering the possible error in determining the rate constants it is estimated that between 0 and 40 per cent of this reaction is due to thiomethoxide and hence that methoxide ions are at least 70 times as reactive as thiomethoxide ions toward chlorodifluoromethane.

In relating the kinetic study to the synthetic reaction where the ratio $(MeS^-)/(MeO^-)$ was 0.16 it seems reasonable to assume that in the latter case practically all of the initial attack on chlorodifluoromethane was by methoxide. As this reaction has already been shown to give an initial difluoromethylene intermediate, essentially all of the sulfur-containing reaction products must have been formed from this intermediate. The following mechanism is proposed for the formation of the sulfur-containing products isolated.

$$CH_3O^- + CHClF_2 \longrightarrow CH_3OH + Cl^- + CF_2$$

$$CH_3S^- + CF_2 \longrightarrow CH_3SCF_2^-$$

$$CH_3SCF_2^- \xrightarrow{CH_3OH} CH_3SCF_2H$$

$$CH_3SCF_2^- \longrightarrow CH_3\text{-}S\text{-}C\text{-}F$$

$$CH_3S + CH_3\text{-}S\text{-}C\text{-}F \xrightarrow{CH_3OH} (CH_3S)_3CH$$

This mechanism is similar to the one proposed earlier for the reaction in methanol in the absence of thiomethoxide. The difluoromethyl methyl sulfide was found to be stable to the reaction conditions and incapable of producing the trimethyl orthothioformate isolated. The only reasonable path left for its formation is through a fluorothiomethyoxymethylene. Whether difluoromethylene and thiomethoxide react by a concerted mechanism or via a difluorothiomethoxycarbanion intermediate is uncertain. The trimethyl orthomonothioformate isolated from the reaction may have been formed from a sulfur- or oxygen-containing methylene intermediate.

Reaction of Difluoromethyl Phenyl Sulfone.--The difluoromethyl phenyl sulfide isolated in the methoxide-catalyzed reaction of chlorodifluoromethane with sodium thiophenoxide was oxidized to the sulfone for the purpose of producing a more stable compound for characterization. Since difluoromethyl phenyl sulfide was found to be essentially unreactive toward sodium methoxide and sodium thiophenoxide, it was of interest to see if the increased electron withdrawing power of the sulfur atom in the $-SO_2-$ group would increase the activity of the difluoromethyl group.

The reaction of difluoromethyl phenyl sulfone with sodium methoxide was carried out at the reflux temperature of methanol. The reaction mixture gave off a gas not

condensed by a water cooled reflux condenser but collected in a Dry Ice trap. The infrared spectrum of this material was identical to that of difluoromethyl methyl ether isolated in the reaction of chlorodifluoromethane with sodium methoxide. The remaining solution yielded benzenesulfinic acid as the major organic product.

From the kinetic study of the reaction of difluoromethyl phenyl sulfone with sodium methoxide we obtained a value of 3.55×10^{-5} l. mole^{-1} sec.$^{-1}$ for the rate constant at 50°. Ziegler and Connor found that bromomethyl p-tolyl sulfone was very unreactive toward nucleophilic reagents and even underwent reduction rather than substitution when treated with sodium ethoxide at 80° for 15 hours to give methyl p-tolyl sulfone (37). The greater reactivity of difluoromethyl phenyl sulfone must be explained by a mechanism other than a nucleophilic displacement reaction.

To determine if an α-elimination was taking place an additional kinetic study was carried out using sodium thiophenoxide. Two kinetic runs were made. One run had an excess of sodium methoxide over that required to neutralize the thiophenol present and the other had an excess of thiophenol present to give a methoxide-free solution. The rate of disappearance of thiophenoxide was found to be dependent on the methoxide concentration. In the run with excess sodium methoxide a second-order rate constant of 3.28×10^{-5}

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(37) W. M. Ziegler and R. Connor, Journal of The American Chemical Society, 62, 2596 (1940).

l. mole^{-1} sec.$^{-1}$ was obtained assuming that the rate of disappearance of difluoromethyl phenyl sulfone depended only on the methoxide concentration. In the run with excess thiophenol the rate constant obtained for the reaction of sodium thiophenoxide with difluoromethyl phenyl sulfone was about 1 x 10^{-7} l. mole^{-1} sec.$^{-1}$. This 200-fold decrease in reaction rate shows that methoxide must catalyze the reaction of difluoromethyl phenyl sulfone with sodium thiophenoxide and that an α-elimination must be taking place. If the sodium thiophenoxide had attacked the sulfone directly in a S_N2 type displacement, we would have expected this strong nucleophilic reagent to have reacted much faster than sodium methoxide, as it has done in other nucleophilic displacement reactions in methanol (34).

The products isolated from the synthetic reaction of difluoromethyl phenyl sulfone with sodium methoxide and sodium thiophenoxide were difluoromethyl methyl ether in 38 per cent yield, difluoromethyl phenyl sulfide in 22 per cent yield and benzenesulfinic acid in over 50 per cent yield, all based on the reacting sulfone. These products give additional evidence for an α-elimination mechanism. Although no orthoesters were isolated, a small amount of a high boiling material suggested that triphenyl orthothioformate was produced.

It was necessary to carry out the deuterium exchange reaction of difluoromethyl phenyl sulfone to see if the first step of the reaction was that of carbanion formation or if

the sulfone was reacting with base by a concerted α-elimination. The deuteriodifluoromethyl phenyl sulfone compound was found to exchange deuterium for protium in the presence of sodium methoxide. The second-order rate constant obtained was 9.54×10^{-4} l. mole^{-1} sec.$^{-1}$ at 0° in methanol. This shows that the first step of the reaction must be carbanion formation and the overall mechanism is as follows:

$$C_6H_5SO_2CF_2H + CH_3O^- \longrightarrow C_6H_5SO_2CF_2^- + CH_3OH$$

$$C_6H_5SO_2CF_2^- \longrightarrow C_6H_5SO_2^- + CF_2$$

$$CF_2 \xrightarrow{CH_3OH} CH_3OCF_2H$$

$$C_6H_5S^- + CF_2 \xrightarrow{CH_3OH} C_6H_5SCF_2H$$

The rate of deuterium exchange of deuteriodifluoromethyl phenyl sulfone was also studied in water at 0°. The rate constant obtained was 6.00×10^{-2} l. mole^{-1} sec.$^{-1}$ with sodium hydroxide as the base. Pearson and coworkers have reported a value of 2.18×10^{-6} l. mole^{-1} sec.$^{-1}$ for the rate constant at 40° for deuterium exchange of 1-deuteriocyclohexyl p-tolyl sulfone in 50 per cent aqueous dioxane (38). The 30,000-fold increase in rate of deuteriodifluoromethyl phenyl sulfone over that of the cyclohexane derivative at a temperature 40° higher must be partially due to fluorine's inductive stabilization of the carbanion. While fluorine is the

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(38) J. Weinstock, J. L. Bernardi and R. G. Pearson, Journal of The American Chemical Society, 80, 4961 (1958).

poorest of the halogens at stabilizing a carbanion (13), it still shows a strong stabilizing effect when compared to hydrogen.

CHAPTER V

RECOMMENDATIONS

It would be of interest to study the mechanism of solvolysis of dimethoxymethyl methyl sulfone in order to explain the mechanism of formation of the orthoesters isolated in this work and also in other homogeneous haloform reactions. From the present study it appears that in the base-catalyzed methanolysis of chlorodifluoromethane the methyl orthoformate isolated came from a fluoromethoxymethylene intermediate. The reaction of the fluoromethoxymethylene intermediate may be as follows:

$$CH_3O\text{-}C\text{-}F \xrightarrow{CH_3OH} (CH_3O)_2C$$

$$(CH_3O)_2C \xrightarrow{CH_3OH} (CH_3O)_3CH$$

The first step in the above reaction mechanism may be concerted as shown or the methoxy group may add to the fluoromethoxymethylene intermediate before it loses fluorine. The presence of two methoxy groups on the carbon atom should make the loss of fluoride a very rapid process, however, if it is not concerted. The methylenes shown may react with available methoxide in addition to methanol as shown.

A test of this mechanism might be made with dimethoxymethyl methyl sulfone. This sulfone might be produced by the hydrogen peroxide oxidation of trimethyl orthomonothioformate

isolated in the reaction of chlorodifluoromethane with sodium methoxide and sodium thiomethoxide. The reaction of dimethoxymethyl methyl sulfone with sodium methoxide and sodium thiophenoxide could be studied. If the reaction of dimethoxymethyl methyl sulfone with thiophenoxide were catalyzed by methoxide, the sulfone might be reacting by an α-elimination mechanism. If this were found to be the case and dimethoxythiophenoxymethane were isolated as a reaction product, the reaction might involve a dimethoxymethylene intermediate. The first-order methanolysis of the sulfone might show whether a dimethoxymethyl carbonium ion is an intermediate in the reaction.

The kinetics of reaction of the compounds difluoronitromethane and difluoroacetonitrile with base might be studied and their rates of carbanion formation measured. These compounds may react by an α-elimination mechanism like that of the difluoromethyl phenyl sulfone. It would be interesting to see how the nitro and cyanide groups affect the rate of basic solvolysis and carbanion formation and if any correlation can be established between them.

APPENDIX

Table 7. Value of f_o for Equation 2 at 35°.[a]

Reaction Time, (hr.)	NaOMe (mole/l.)	Cl^- formed (mole/l.)	f_o
0.0	0.0321		
4.0	.0179	0.0121	0.0898
4.9	.0146	.0151	.0877
7.1	.0103	.0185	.0923
11.0	.0057	.0230	.0741
20.1	.0045	.0242	.0721
23.5	.0038	.0244	.0802
27.1	.0026	.0257	.0736
43.2	.0032	.0255	.0672

[a] $(CHClF_2)_o$ = 0.036 M

Table 8. Reaction of Chlorodifluoromethane with Sodium Thiophenoxide at 35°.[a]

Reaction Time, (sec.)	Thiophenol (mole/l.)	Thiophenoxide (mole/l.)	10^6 k, l. $mole^{-1}$ $sec.^{-1}$
0	0.0158	0.2161	
13,380	.0119	.2177	5[b]
35,112	.0107	.2158	5

[a] $(CHClF_2)_o$ = 0.1484 M

[b] The k's were calculated using equation 8 where a = $(CHClF_2)_o$, b = $(C_6H_5S^-)_o$, x = $\Delta(C_6H_5S^-) + \Delta(C_6H_5SH)$ at time t, t in sec., and n = 1.

Table 9. Reaction of Chlorodifluoromethane with Sodium Methoxide and Sodium Thiomethoxide at 34.5°.[a]

Reaction Time, (sec.)	1.036 N H_2SO_4 (ml.)	0.2500 M I_2 (ml.)
120	4.05	4.08
1,650	3.70	3.60
5,520	3.08	3.12
9,540	2.80	3.00
28,440	2.52	2.70
39,920	2.50	2.58

[a] $(CHClF_2)_o$ = 0.1502 M

Table 10. Reaction of Chlorodifluoromethane with Sodium Thiomethoxide and Excess Methanethiol at 34.5°.[a]

Reaction Time, (sec.)	1.036 N H_2SO_4 (ml.)	0.2500 M I_2 (ml.)
120	4.88	12.90
2,310	4.80	12.77
22,860	4.48	12.10
26,460	4.42	12.05
66,480	4.10	10.85
157,200	3.71	10.18

[a] $(CHClF_2)_o$ = 0.1502 M

Table 11. Reaction of Difluoromethyl Methyl Sulfide with Sodium Methoxide and Sodium Thiomethoxide at 50°.[a]

Reaction Time, (days)	1.036 N H_2SO_4 (ml.)	0.0500 M I_2 (ml.)
0	11.73	45.82
10	11.58	45.84
22	11.60	45.75

[a] $(CH_3SCF_2H)_o$ = 0.231 M

Table 12. Reaction of Difluoromethyl Phenyl Sulfone with Sodium Thiophenoxide at 50.4°.[a]

Reaction Time, (sec.)	C_6H_5SH (mole/l.)	$C_6H_5S^-$ (mole/l.)
0	0.0137	0.1734
41,940	.0133	.1723
328,320	.0150	.1706
1,180,320	.0107[b]	.1690[b]

[a] $(C_6H_5SO_2CF_2H)_o$ = 0.1379 M

[b] Total thiophenol reacting accounts for only 4.0 per cent reaction.

Table 13. Reaction of Difluoromethyl Phenyl Sulfone with Excess Sodium Methoxide at 50.4°.[a]

Reaction Time, (sec.)	MeO^- (mole/l.)	n
0	0.6168	
428,000	.5169	1.45[b]
1,037,000	.5167	1.45

[a] $(C_6H_5SO_2CF_2H)_o$ = 0.0690 M

[b] Moles of Sodium Methoxide reacting per mole of $C_6H_5SO_2CF_2H$.

Table 14. Extinction Coefficients for $C_6H_5SO_2CF_2H$ and $C_6H_5SO_2CF_2D$ in Carbon Disulfide.

Wave Length (microns)	E for $C_6H_5SO_2CF_2H$ (0.025 mm. cell)	E for $C_6H_5SO_2CF_2D$ (0.025 mm. cell)
7.674	2.565 ± 0.027	0.714 ± 0.007
8.361	0.218 ± .006	4.067 ± .031
8.593	3.973 ± .030	1.226 ± .007
12.093	1.011 ± .001	0.172 ± .001
12.763	0.148 ± .057	1.996 ± .014

Table 15. Rate of Deuterium Exchange of $C_6H_5SO_2CF_2D$ in Methanol at 0°.[a]

Reaction Time, (sec.)	$C_6H_5SO_2CF_2D$ per cent	10^5 k, (sec.$^{-1}$)
12,600	71.9[b]	
17,700	64.0	2.29
25,980	52.0	2.36
34,560	42.9	2.35
39,420	38.5	2.33
51,060	30.7	2.21
	Av.	2.31 ± 0.04[c]

[a] $(C_6H_5SO_2CF_2D)_o$ = 0.0690 M, $(NaOMe)_o$ = 0.0237 M

[b] This point used as zero reaction point. All values calculated from absorption at 8.361 μ and 8.593 μ.

[c] Second-order rate (9.71 x 10^{-4} l./mole sec.) obtained by dividing by NaOMe concentration.

Table 16. Reaction of Difluoromethyl Phenyl Sulfide with Sodium Methoxide and Sodium Thiophenoxide at 50°.[a]

Reaction Time, (days)	MeO^- (mole/l.)	$C_6H_5S^-$ (mole/l.)
0	0.712	0.925
7	.712	.916
23	.693[b]	.908[b]

[a] $(C_6H_5SCF_2H)_o$ = 0.512 M

[b] This corresponds to less than 7.0 per cent reaction of difluoromethyl phenyl sulfide.

Table 17. Rate of Deuterium Exchange of $C_6H_5SO_2CF_2D$ in Methanol at 0°.[a]

Reaction Time, (sec.)	$C_6H_5SO_2CF_2D$ per cent	10^5 k, (sec.$^{-1}$)
1,800	83.3[b]	
3,600	73.4	7.04
7,530	51.2	6.65
10,800	45.4	6.75
14,430	38.7	6.08
18,000	27.8	6.77
	Av.	6.66 ± 0.23[c]

[a] $(C_6H_5SO_2CF_2D)_o$ = 0.0690 M, $(NaOMe)_o$ = 0.0711 M

[b] This point used as zero reaction point. All values calculated from absorption at 8.361μ and 8.593μ.

[c] Second-order rate constant (9.37×10^{-4} l./mole sec.) was obtained by dividing by NaOMe concentration.

Table 18. Rate of Deuterium Exchange of $C_6H_5SO_2CF_2D$ in Water at 0°.[a]

Reaction Time, (sec.)	$C_6H_5SO_2CF_2D$ per cent	10^5 k, (sec.$^{-1}$)
3,620	77.6[b]	
6,780	64.8	5.67
13,480	44.3	5.68
19,260	32.8	5.51
25,630	24.8	5.44
	Av.	5.57 ± 0.10[c]

[a] $(C_6H_5SO_2CF_2D)_o$ = 0.00621 M, $(NaOH)_o$ = 0.00089 M

[b] This point used as zero reaction point. All values calculated from absorption at 8.361 μ and 8.593 μ.

[c] Second-order rate constant (6.25×10^{-2} l./mole sec.) was obtained by dividing by NaOH concentration.

Table 19. Rate of Deuterium Exchange of $C_6H_5SO_2CF_2D$ in Water at 0°.[a]

Reaction Time, (sec.)	$C_6H_5SO_2CF_2D$ per cent	10^5 k, ($sec.^{-1}$)
2,700	76.2[b]	
4,540	67.5	6.59
7,720	51.9	6.52
12,810	35.4	6.99
16,710	26.7	7.05
	Av.	6.79 ± 0.23[c]

[a] $(C_6H_5SO_2CF_2D)_o$ = 0.00621 M, $(NaOH)_o$ = 0.00117

[b] Used as zero reaction point. All values calculated from absorption at 8.361μ and 8.593μ.

[c] Second-order rate constant (5.82 x 10^{-2} l./mole sec.) was obtained by dividing by NaOH concentration.

Table 20. Data for Calculating the Indicator Constant K_{In} in Methanol at 25°.

1.00 M $NaClO_4$ (ml.)	0.763 M NaOMe (ml.)	3×10^{-4} M Thymol Blue[a] (ml.)	Optical Density (5850 Å)	$10^3 K_{In}$
	2.00	1.00	0.364[b]	
	4.00	1.00	.364	
5.00	2.00	1.00	.365	
5.00	4.00	1.00	.364	
5.00	.10	1.00	.349	2.85
3.00	.10	1.00	.343	4.16
2.00	.10	1.00	.335	5.95
1.00	.10	1.00	.328	7.63
.50	.10	1.00	.326	8.15
	.10	1.00	.310	12.25
5.00	.025	1.00	.275	3.01
3.00	.025	1.00	.248	5.10
2.00	.025	1.00	.242	5.90
1.00	.025	1.00	.226	7.63
		1.00	.001	

[a]The extinction coefficient for thymol blue was determined to be approximately 53,800 for the basic form at 5850 Å. Since the neutral form showed negligible absorption at this wave length, the optical density readings were used as direct readings for the concentration of the basic form of the indicator.

[b]The solutions were made in a 10 ml. volumetric flask which was filled to the mark with methanol after the reagents were added.

Table 21. Data for Calculating the Equilibrium Constant K_e in Methanol at 25°.

1.00 M $NaClO_4$ (ml.)	0.7906 M NaOMe (ml.)	3×10^{-4} M Thymol Blue[a] (ml.)	0.590 M CH_3SH (ml.)	Optical Density (5850 Å)	K_e
	3.0	2.00		0.658[b]	
	6.0	2.00		.656	
13.00	1.00	2.00	9.00	.425	349[c]
13.00	.50	2.00	9.00	.305	340
10.00	1.00	2.00	9.00	.424	271
10.00	.50	2.00	9.00	.302	257
8.00	1.00	2.00	9.00	.425	220
8.00	.50	2.00	9.00	.300	213

[a]See footnote a Table 20.

[b]The solutions were made in a 25 ml. volumetric flask which was filled to the mark with methanol after the reagents were added.

[c]Calculated using values of K_{In} obtained from Figure 1.

Table 22. Data for Calculating the Equilibrium Constant K_e in Methanol at 25°.

1.00 M $NaClO_4$ (ml.)	0.5550 M NaOMe (ml.)	3×10^{-4} M Thymol Blue[a] (ml.)	0.460 M CH_3SH (ml.)	Optical Density (5850 Å)	K_e
	14.0	1.00		0.505[b]	
5.00	1.00	1.00	3.00	.444	219[c]
5.00	1.00	1.00	8.00	.334	226
7.00	1.00	1.00	6.00	.370	318

[a]See footnote a Table 20.

[b]The solutions were made in a 15 ml. volumetric flask which was filled to the mark with methanol after the reagents were added.

[c]Calculated using values of K_{In} obtained from Figure 1.

Table 23. Data for Calculating the Equilibrium Constant K_e in Methanol at 25°.

0.3134 M NaOMe (ml.)	3×10^{-4} M Thymol Blue[a] (ml.)	0.3840 M CH_3SH (ml.)	Optical Density (5850 Å)	K_e
10.00	2.00		0.880[b]	
1.00	2.00	3.00	.620	144[c]
1.00	2.00	6.00	.498	120
1.00	2.00	9.00	.369	142
1.00	2.00	12.00	.300	146

[a]See footnote a Table 20.

[b]The solutions were made in a 15 ml. volumetric flask which was filled to the mark with methanol after the reagents were added.

[c]Calculated using values of K_{In} obtained from Figure 1.

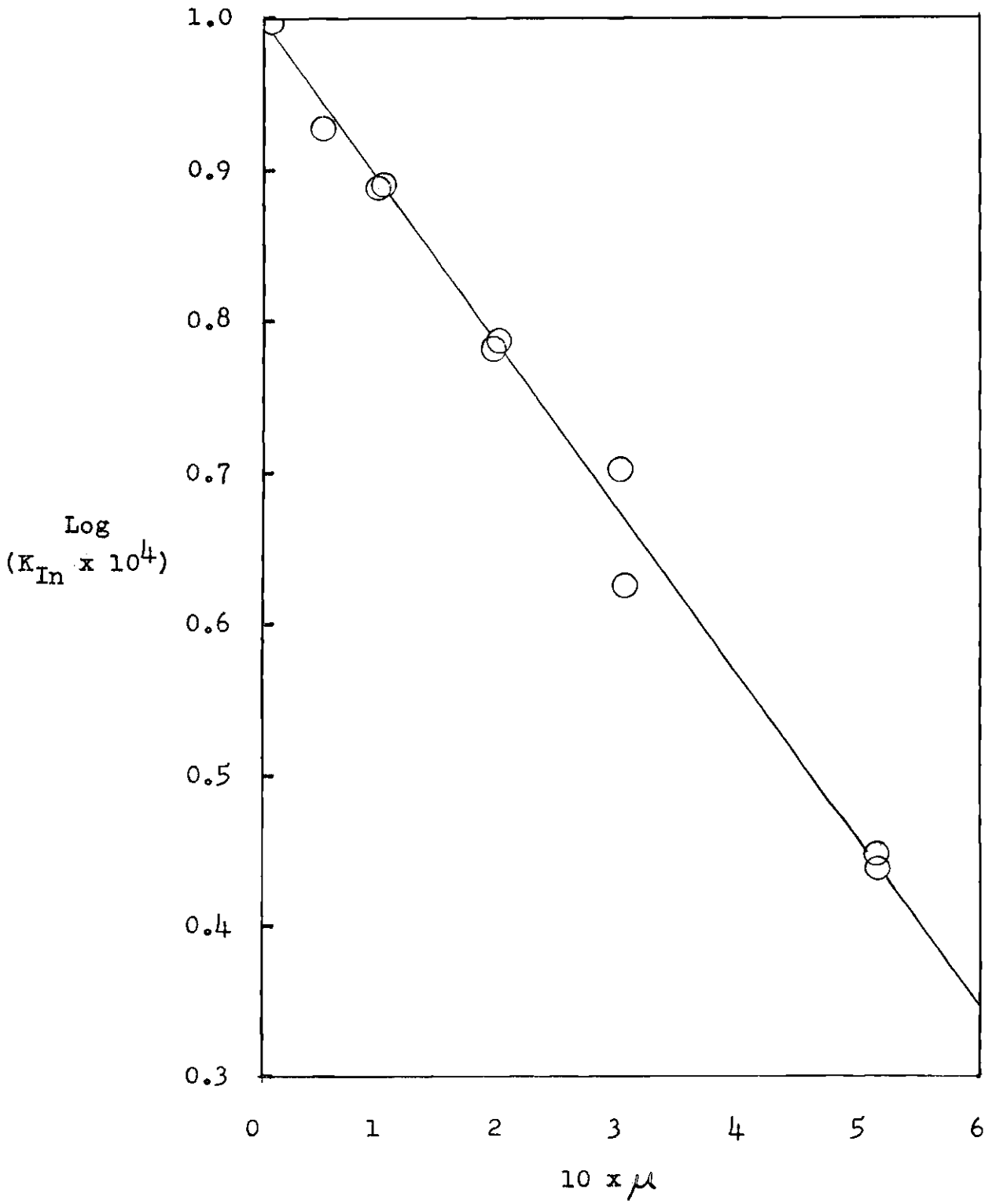

Figure 1. Log K_{In} versus Ionic Strength

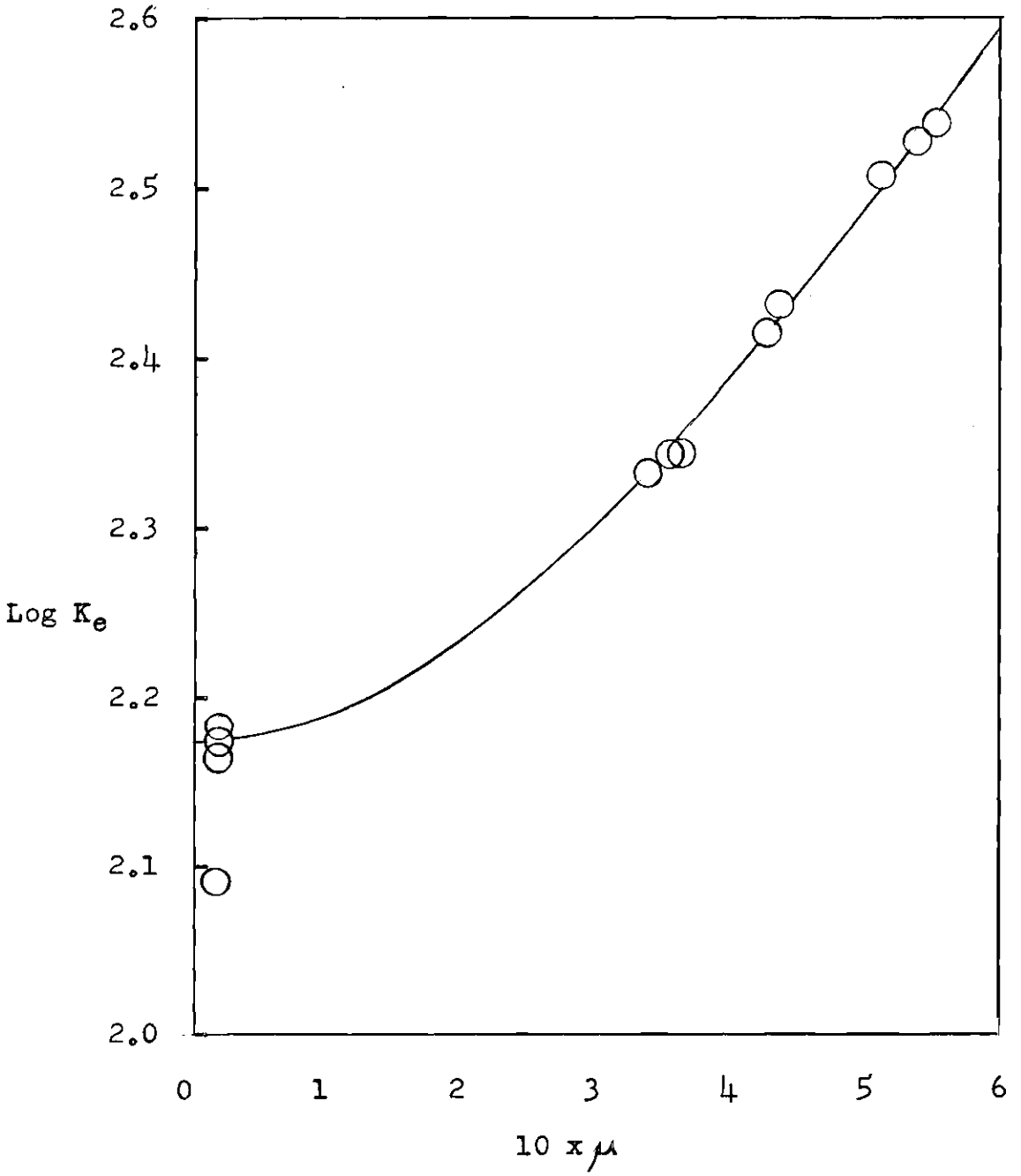

Figure 2. Log K_e versus Ionic Strength

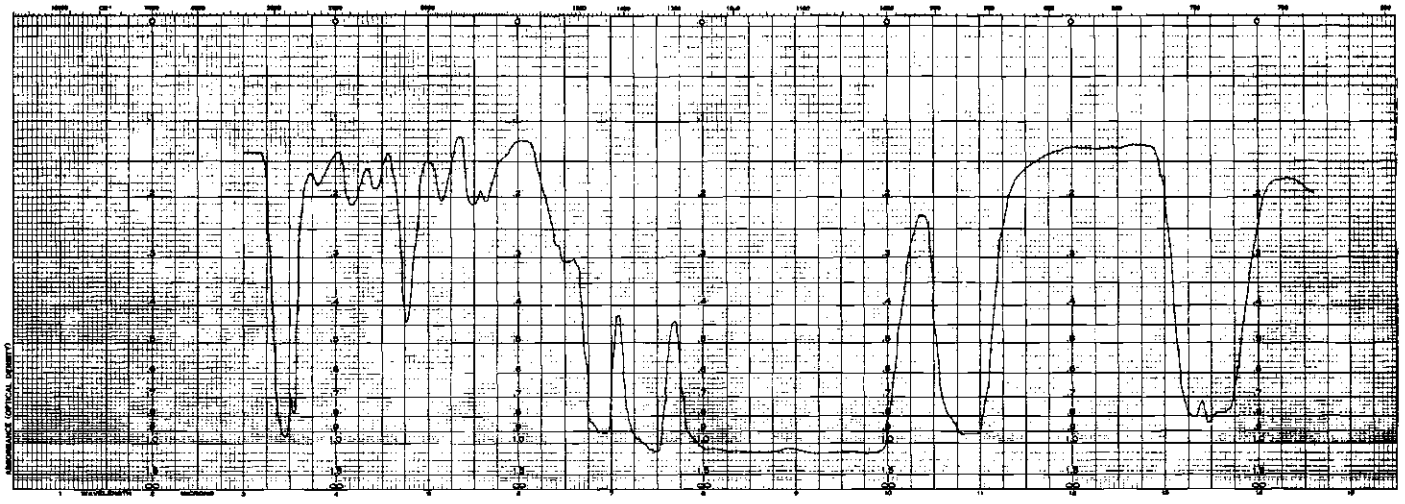

Figure 3. Infrared Spectrum of Difluoromethyl Methyl Ether.
(gas at 745 mm., 10 cm. cell thickness).

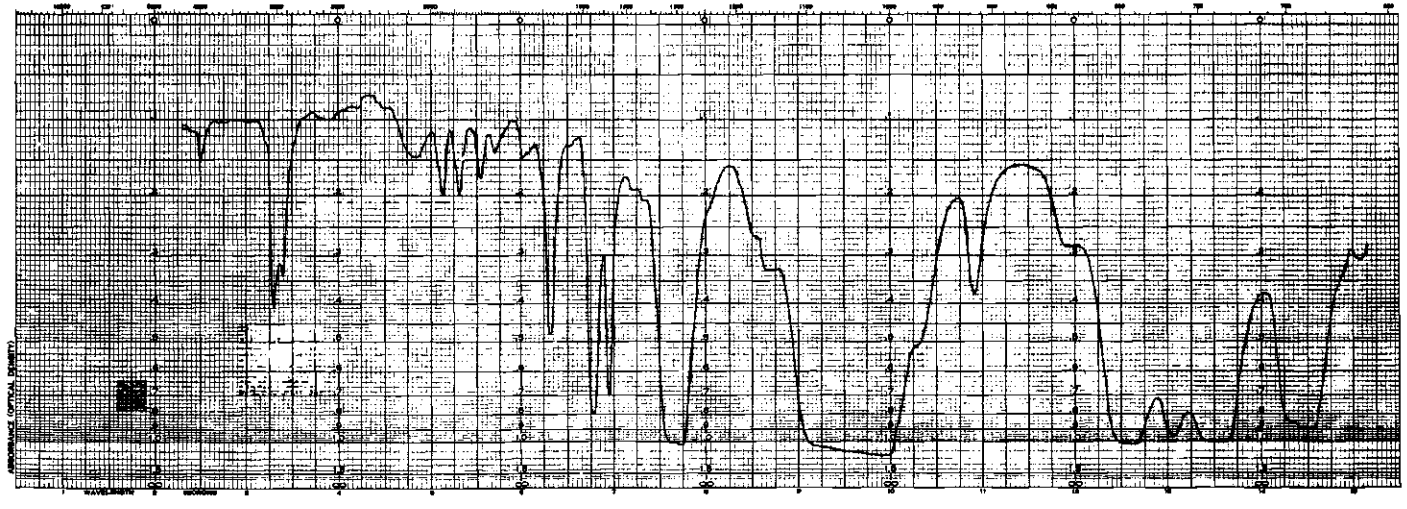

Figure 4. Infrared Spectrum of Difluoromethyl Phenyl Sulfide.
(pure liquid, 0.025 mm. cell thickness).

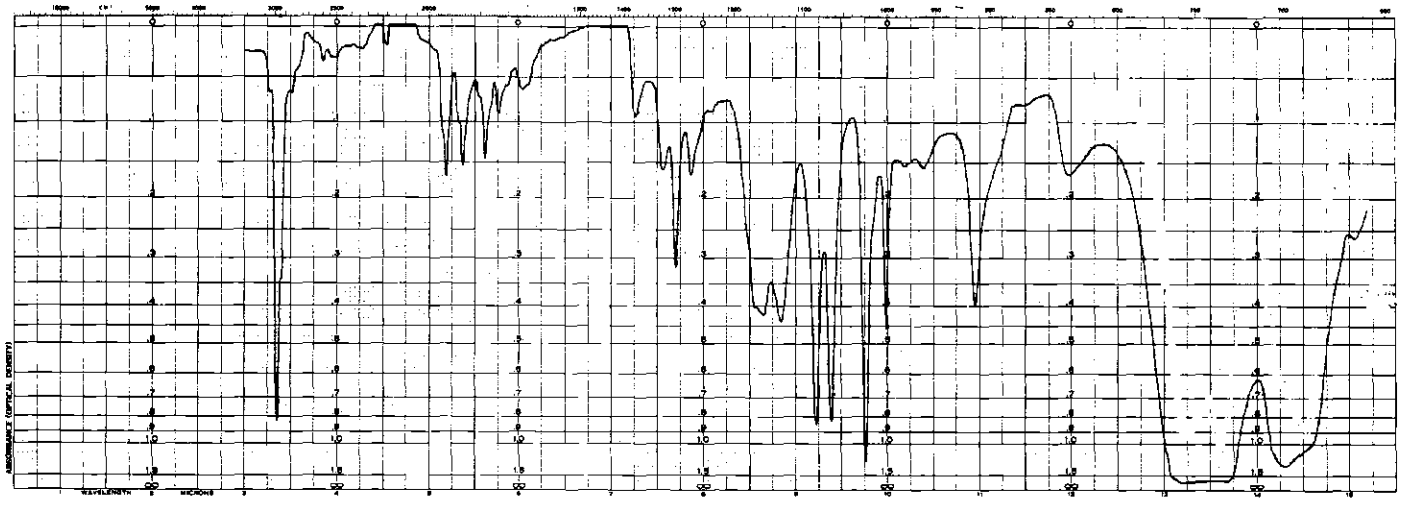

Figure 5. Infrared Spectrum of Triphenyl Orthothioformate.
(carbon disulfide solution, 0.5 mm. cell thickness).

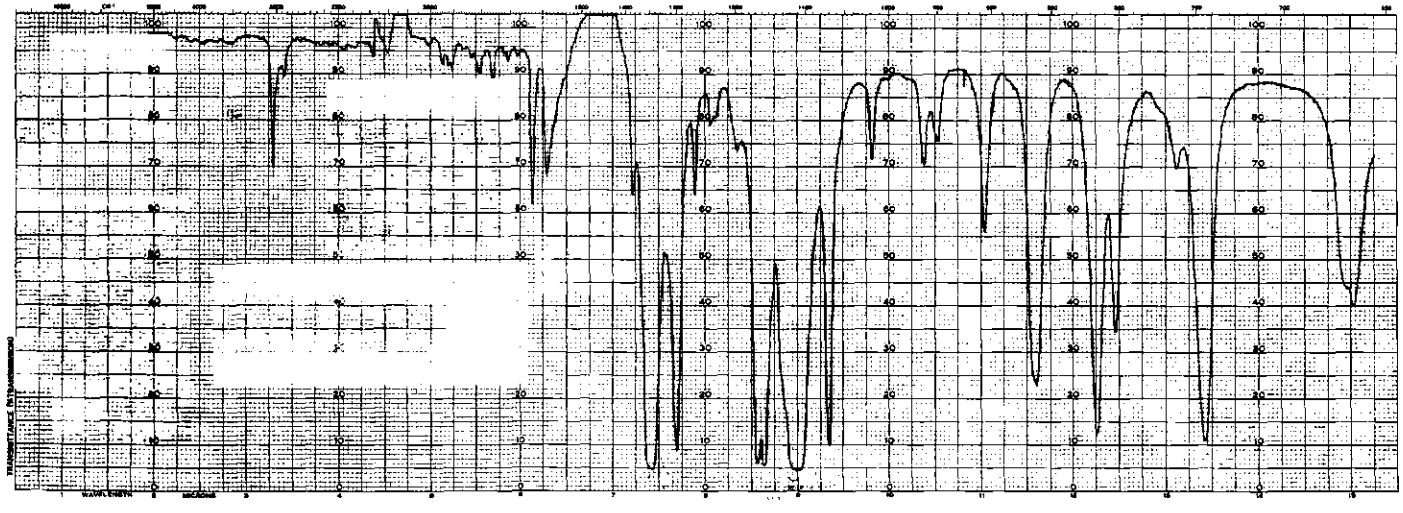

Figure 6. Infrared Spectrum of Difluoromethyl 2-Napthyl Sulfone.
(carbon disulfide solution, 0.1 mm. cell thickness).

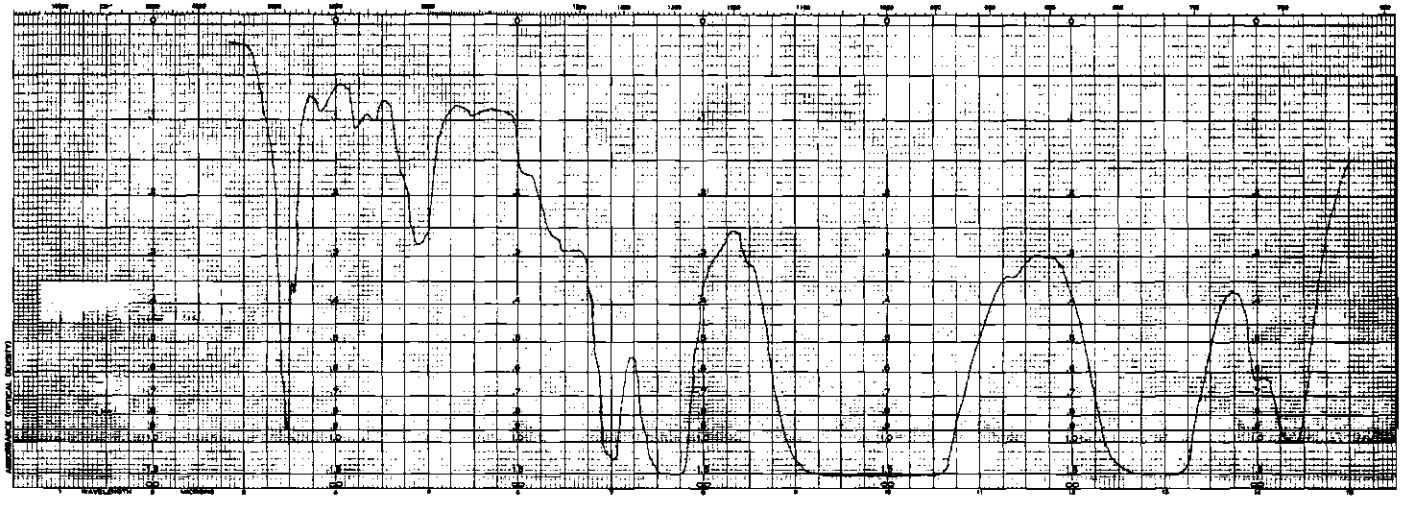

Figure 7. Infrared Spectrum of Difluoromethyl Methyl Sulfide.
(pure liquid, 0.025 mm. cell thickness).

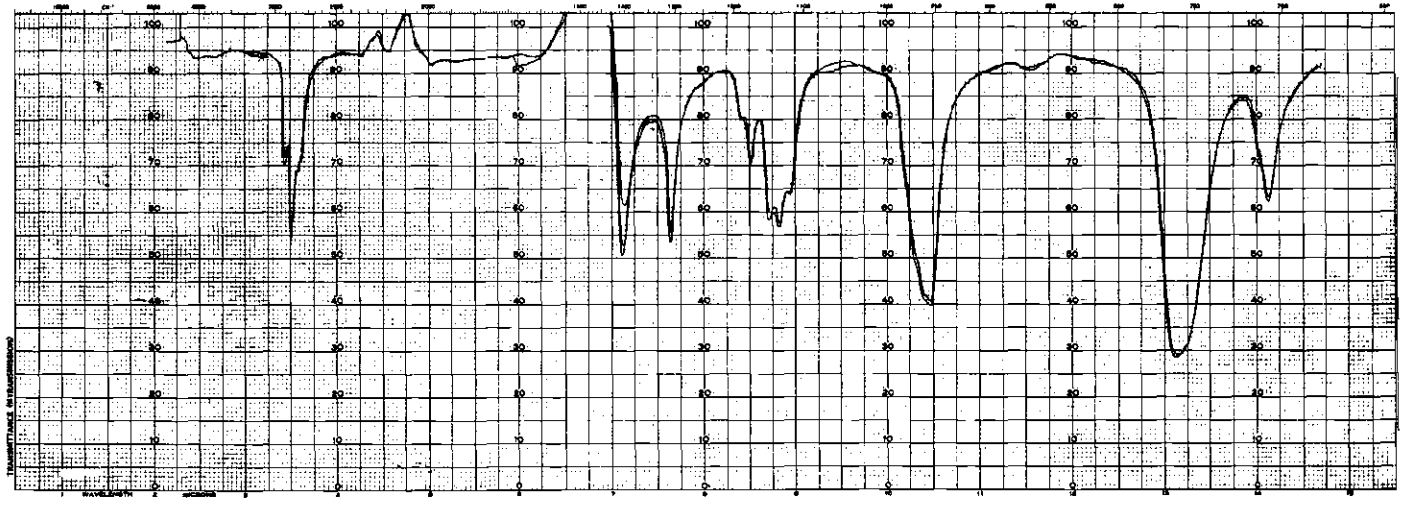

Figure 8. Infrared Spectrum of Trimethyl Orthothioformate.
(carbon disulfide solution, 0.1 mm. cell thickness).

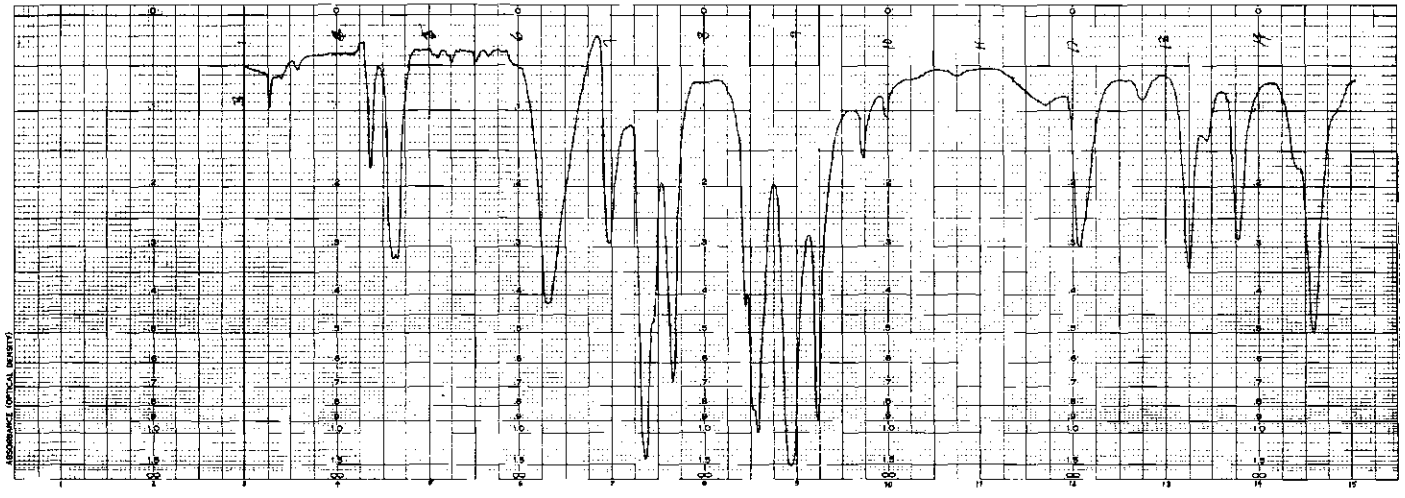

Figure 9. Infrared Spectrum of Difluoromethyl Phenyl Sulfone.
(carbon disulfide solution, 0.025 mm. cell thickness).

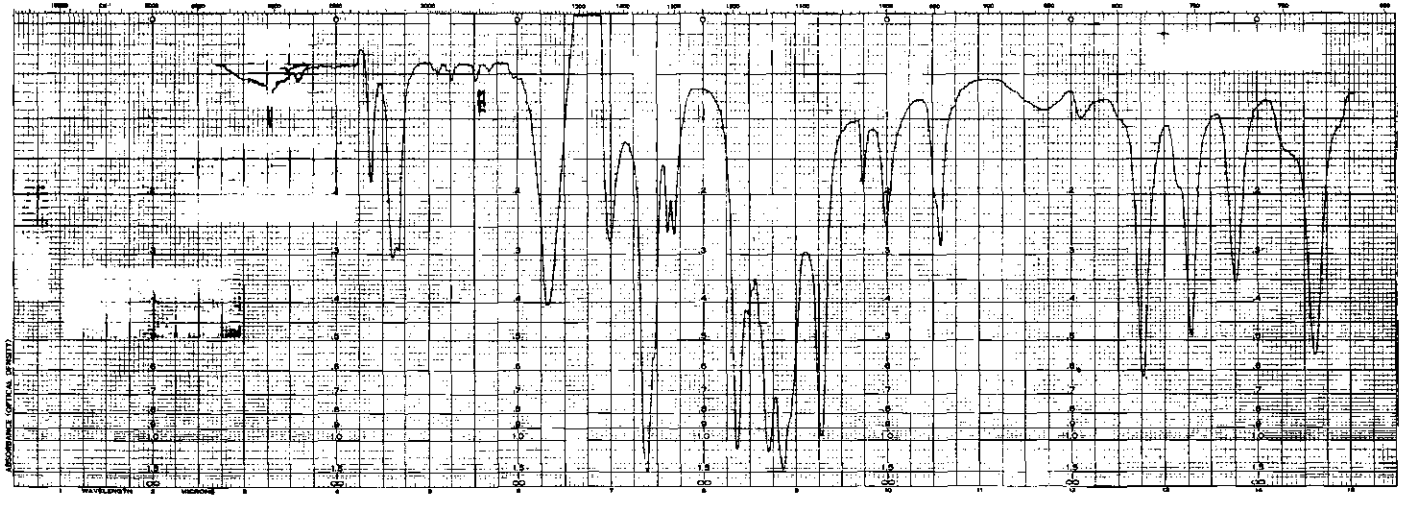

Figure 10. Infrared Spectrum of Deuteriodifluoromethyl Phenyl Sulfone.
(carbon disulfide solution, 0.025 mm. cell thickness).

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VITA

John Jefferson Porter, the son of Mr. and Mrs. William Jackson Porter, was born in East Orange, New Jersey, on February 15, 1932. When he was four years old his family moved to Atlanta, Georgia, where they currently reside. He attended both Fulton and Dekalb County primary and secondary schools and was graduated from Chamblee High School in 1950. After this he was employed at Sears Roebuck and Company and attended the Atlanta Division of the University of Georgia. At the beginning of the year 1952 he enrolled full time in the School of Chemical Engineering of the Georgia Institute of Technology. He received his Bachelor degree in Chemical Engineering, co-operative plan, in June of 1956, whereupon he entered the Graduate Division in the School of Chemistry. On June 6, 1959, he was married to Patricia Jane West of Maryville, Tennessee.